=> fil wpix
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=> d all abeq tech tot

L39 ANSWER 1 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-360082 [31] WPIX
DNC C1999-106780
TI Removing viruses from factor VIII solution - by filtration on nanoporous hydrophilic filter.
DC B04
IN **CHTOUROU, A S; NOGRE, M; PORTE, P;**
CHTOUROU, A
PA (FRFR-N) LAB FR DU FRACTIONNEMENT & BIOTECHNOLOGI
CYC 23
PI FR 2772381 A1 19990618 (199931)* 24p C07K001-34
WO 9931138 A1 19990624 (199932) FR C07K014-755
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP US
AU 9915681 A 19990705 (199948) C07K014-755
EP 1037923 A1 20000927 (200048) FR C07K014-755
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT FR 2772381 A1 FR 1997-15888 19971215; WO 9931138 A1 WO 1998-FR2715 19981214; AU 9915681 A AU 1999-15681 19981214; EP 1037923 A1 EP 1998-959975 19981214, WO 1998-FR2715 19981214
FDT AU 9915681 A Based on WO 9931138; EP 1037923 A1 Based on WO 9931138
PRAI FR 1997-15888 19971215
IC ICM C07K001-34; C07K014-755
ICS **A61K038-37**
AB FR 2772381 A UPAB: 19990806
Process for preparing a virus-safened solution of factor VIII (FVIII) containing no high-molecular-weight von Willebrand factor (vWF) comprises (a) preparing a high-purity FVIII solution containing or not containing high-molecular-weight vWF-FVIII complexes, (b) dissociating any high-molecular-weight vWF-FVIII complexes in the solution, and (c) filtering the solution on a hydrophilic filter having a pore size as low as 15 nm.
USE - for treating haemophilia A.
ADVANTAGE - The process removes both high-molecular-weight vWF and viruses, including small viruses such as parvovirus B19.
Dwg.0/1
FS CPI
FA AB
MC CPI: B04-H19; B14-F08

L39 ANSWER 2 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-277588 [23] WPIX
DNC C1999-081623
TI Preparation of pure virus free immunoglobulin by nanofiltration - using

alcohol fractionation and high ionic strength buffer and nonionic detergent, also other protein preparations.

DC A96 B04 D16

IN OULUNDSEN, G E; QUINTON, G J; VAN HOLTEN, R W

PA (MIFI) MILLIPORE CORP; (ORTH) ORTHO DIAGNOSTIC SYSTEMS INC; (ORTH) ORTHO CLINICAL DIAGNOSTICS INC

CYC 26

PI WO 9919343 A1 19990422 (199923)* EN 66p C07K001-00
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA CN JP KR NO
AU 9910817 A 19990503 (199937) C07K001-00
US 6096872 A 20000801 (200039) A61K039-395
NO 2000001949 A 20000614 (200040) C07K016-00
EP 1030862 A1 20000830 (200042) EN C07K001-00
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
CN 1279688 A 20010110 (200128) C07K001-00
KR 2001015753 A 20010226 (200156) C07K016-00

ADT WO 9919343 A1 WO 1998-US21574 19981014; AU 9910817 A AU 1999-10817 19981014; US 6096872 A **US 1997-950157 19971014**; NO 2000001949 A WO 1998-US21574 19981014, NO 2000-1949 20000413; EP 1030862 A1 EP 1998-953439 19981014, WO 1998-US21574 19981014; CN 1279688 A CN 1998-811286 19981014; KR 2001015753 A KR 2000-703939 20000412

FDT AU 9910817 A Based on WO 9919343; EP 1030862 A1 Based on WO 9919343

PRAI **US 1997-950157 19971014**

IC ICM A61K039-395; C07K001-00; C07K016-00
ICS A23J001-00; C07K001-30; **C07K001-34**; C07K014-00; C07K016-34; C07K017-00

AB WO 9919343 A UPAB: 19990624

NOVELTY - Preparation of pure virus free immunoglobulin by nanofiltration, is new.

DETAILED DESCRIPTION - Process for manufacture of substantially pure protein, comprising: (a) isolating a protein from plasma; (b) resuspending in buffer; (c) mixing with processing aids; and (d) performing a nanofiltration on the isolate.

USE - The process is used to yield a substantially pure product for injection, free from viruses, which are removed in the size-exclusion ultrafiltration. These viruses include both enveloped (e.g., HIV, hepatitis B) and non-enveloped (e.g., hepatitis A, parvovirus B19). The process can be applied to large globular proteins, including albumins, immunoglobulins and their fragments, **blood coagulation factors** e.g., **factors VIII**, IX, and XI, growth hormones, apolipoproteins, and enzymes, all either naturally occurring or genetically engineered. Most notably, the process applies to the immunoglobulins (Ig), as both monoclonal and polyclonal antibodies; particularly the anti-D Ig, more specifically RhoGAM or #MICRhoGAM . These are used in prevention of hemolytic disease of the newborn, being given at about 26-28 weeks; and in the treatment of women who may have abortions and miscarriages at 12 weeks or earlier.

ADVANTAGE - The process yields a substantially pure product safe for injection, free from viruses (prions are also mentioned), which are removed in the size-exclusion ultrafiltration. The combination of high ionic strength buffer and nonionic excipient shifts the protein equilibrium away from dimer, trimer, and aggregate formation, a serious problem in prior art; these polymers pass through nanofilters suitable for removing virus particles only with difficulty or not at all. (The only safe procedure for preparation of these proteins free from virus in prior art has been from plasma carefully selected and proved viral negative). Higher concentrations of protein can be used without association difficulties, reducing processing time, and the yield is greater; smaller pore nanofilters can be used with better assurance of viral clearance of the smaller non-enveloped virus.

Dwg.0/5

FS CPI

FA AB

MC CPI: A12-L04; A12-V03B; B04-G01; B11-B; D05-H13

L39 ANSWER 3 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1998-034929 [04] WPIX
DNC C1998-011842
TI Pure, non-immunogenic **Factor-VIII** composition preparation - using 2-stage viral inactivation of **Factor-VIII** solution by treatment with phosphate and detergent followed by heating, used for treating haemophilia.
DC B04 D16
IN BUCCI, E; DICHTELMULLER, H; KLOFT, M; KOTITSCHKE, R; LOEBNAU, W; OTT, G; RUDNICK, D; DICHTELMUELLER, H
PA (BIOT) BIOTEST PHARMA GMBH
CYC 20
PI EP 812858 A1 19971217 (199804)* DE 16p C07K014-755 <--
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
DE 19623293 A1 19971218 (199805) 12p C07K014-755 <--
CZ 9701774 A3 19971217 (199807) C07K014-755 <--
HU 9700987 A2 19980302 (199821) A61K035-16
DE 19623293 C2 19981022 (199846) C07K014-755 <--
ADT EP 812858 A1 **EP 1997-109314 19970609**; DE 19623293 A1 **DE 1996-19623293 19960611**; CZ 9701774 A3 **CZ 1997-1774 19970609** ; HU 9700987 A2 **HU 1997-987 19970603**; DE 19623293 C2 **DE 1996-19623293 19960611**
PRAI **DE 1996-19623293 19960611**
IC ICM A61K035-16; **C07K014-755**
ICS **A61K038-37**; C07K001-18; **C07K001-34**
AB EP 812858 A UPAB: 19980126
Preparation of a non-immunogenic composition (I) containing **Factor VIII** (F8) comprises:
(a) treatment of a solution of F8 with tri-(n-butyl) phosphate (TNBP) and detergent, and
(b) heat treatment of a freeze-dried material containing F8 at 100 deg. C for 15-120 minutes, such that the residual moisture content after the heat treatment is 0.3-1.8 wt.%.
Also claimed is (I).
USE - F8 is used for treating haemophilia.
ADVANTAGE - (I) containing highly pure, doubly virus-inactivated F8 can be obtained from human **blood** plasma using a 2-stage virus inactivation and purification process involving no use of stabilisers.
Enveloped and non-enveloped viruses are effectively inactivated. Typically the HIV-1 reduction **factor** (log 10) is > 16.2. Heat treatment under the present conditions causes no significant activity loss.
F8 is typically enriched by a **factor** of 104 compared with the starting plasma.
Dwg.0/3
FS CPI
FA AB
MC CPI: **B04-H19**; B14-F08; D05-H13; D05-H17A

L39 ANSWER 4 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1997-457355 [42] WPIX
DNC C1997-145987
TI Separating solids from mixture of bio-molecules, especially applied to isolation of albumin, immuno-globin(s) etc. from blood products - by filtration in presence of cellulosic filter aid that does not leach aluminium or generate prekallikrein activity.
DC B04 D16 J01
IN DAVIES, J R; JOHNSTON, A; TURNER, P J; WILKIE, B J
PA (CSLC-N) CSL LTD
CYC 78
PI WO 9732654 A1 19970912 (199742)* EN 38p B01D037-02 <--
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU

AU 9720864	A	19970922 (199804)			B01D037-02	<--
ZA 9701988	A	19980128 (199810)		37p	B01D000-00	
EP 885046	A1	19981223 (199904)	EN		B01D037-02	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT SE SI						
CN 1213326	A	19990407 (199932)			B01D037-02	
AU 710566	B	19990923 (199951)			B01D037-02	
NZ 331367	A	20000428 (200027)			B01D037-02	
JP 2000506843	W	20000606 (200035)		39p	A61K035-12	
KR 99087623	A	19991227 (200059)			B01D037-02	

ADT WO 9732654 A1 **WO 1997-AU139 19970306**; AU 9720864 A **AU 1997-20864 19970306**; ZA 9701988 A **ZA 1997-1988 19970307**; EP 885046 A1 **EP 1997-906031 19970306, WO 1997-AU139 19970306**; CN 1213326 A **CN 1997-192886 19970306**; AU 710566 B **AU 1997-20864 19970306**; NZ 331367 A **NZ 1997-331367 19970306, WO 1997-AU139 19970306**; JP 2000506843 W **JP 1997-531258 19970306, WO 1997-AU139 19970306**; KR 99087623 A **WO 1997-AU139 19970306**, KR 1998-707072 19980908

FDT AU 9720864 A Based on WO 9732654; EP 885046 A1 Based on WO 9732654; AU 710566 B Previous Publ. AU 9720864, Based on WO 9732654; NZ 331367 A Based on WO 9732654; JP 2000506843 W Based on WO 9732654; KR 99087623 A Based on WO 9732654

PRAI **AU 1996-8585 19960308**

REP 2.Jnl.Ref; JP 54058270; JP 63042711; US 4416777; WO 8303198; WO 9005461

IC ICM A61K035-12; B01D000-00; B01D037-02
ICS A61K035-14; A61K038-00; A61K038-43; A61K038-48; A61K039-395; B01D039-04; B01D039-16; B01D039-18; **C07K001-34**

AB WO 9732654 A UPAB: 19971021

Solids (A) are separated from a mixture of biomolecules (B) by combining the mixture with a cellulose-based filter aid (C), then passing or pumping the resulting slurry through a filter vessel or mesh. Alternatively a filter mesh is precoated with (C) and the mixture passed through it. Also new are (B) produced this way.

The mixture of (B) is **blood**, frozen plasma, cryosupernatant or a plasma fraction, such as a Cohn or Oncley fraction, and (A) is precipitated, aggregated or complexed, or bound to an insoluble carrier such as fumed silica. Particularly (A) is produced as the result of at least 1 ethanol/acetate precipitation or treatment with fumed silica. (C) (i) facilitates flow of feed mixture through the filter; and (ii) does not leach aluminium nor (iii) generate PKA to above acceptable standards. Specified (C) are 'Diacel' (RTM) 150 or 200; 'Arbocel' (RTM) 200 and 'Vitacel' (RTM) 200. A preferred isolated (B) is albumin containing < 3 (preferably 0.3) wt.% lipoprotein, and with levels of PKA, PKA-C1 esterase, kallikrein and aluminium within acceptable levels, specifically < 10 mu g/ml aluminium, 5 IU/ml PKA and 10 IU/ml PKA-C1 esterase.

USE - Isolated (B), preferably **blood** proteins (especially albumin but also lipoprotein, immunoglobulin (Ig), euglobulin, **factor VIII**, prothrombin complex or antithrombin III) are used in therapeutic or prophylactic treatment of humans and other mammals.

ADVANTAGE - (C) does not leach aluminium nor generate prekallikrein activity (PKA) in the product, and is available with consistent quality (contrast diatomaceous earth, which is also abrasive).

Dwg.0/2

FS CPI
FA AB
MC CPI: B04-B04D2; **B04-H19**; D05-H13; J01-F02

L39 ANSWER 5 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1996-371944 [38] WPIX
DNC C1996-118116
TI Removing viruses from protein soln. by filtration - after reaction with receptor to increase particle size, allows elimination of even small viruses while retaining larger proteins in soln..
DC B04 D16
IN BERNHARDT, D; GRONER, A; NOWAK, T; GROENER, A
PA (CENT-N) CENTEON PHARMA GMBH; (BEHW) BEHRINGWERKE AG

CYC 19
PI DE 19504211 A1 19960814 (199638)* 4p C07K001-34 <--
EP 727226 A2 19960821 (199638) DE 5p A61L002-02 <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE
AU 9644401 A 19960815 (199641) C07K001-34 <--
JP 08242849 A 19960924 (199648) 5p C12N007-02 <--
CA 2169122 A 19960810 (199649) C12N007-02 <--
AU 708757 B 19990812 (199944) C07K001-34 <--
ADT DE 19504211 A1 **DE 1995-19504211 19950209**; EP 727226 A2 **EP 1996-100268 19960110**; AU 9644401 A **AU 1996-44401 19960207**; JP 08242849 A **JP 1996-22195 19960208**; CA 2169122 A **CA 1996-2169122 19960208**; AU 708757 B **AU 1996-44401 19960207**
FDT AU 708757 B Previous Publ. AU 9644401
PRAI **DE 1995-19504211 19950209**
REP No-SR.Pub
IC ICM A61L002-02; **C07K001-34**; C12N007-02
ICS B01D061-14; B01D063-02
ICA C12M003-06
AB DE 19504211 A UPAB: 19960924
Removal of viruses from protein soln. comprises binding them to receptors, to increase their size, then retaining them by filtration.
USE - The method is used to decontaminate pooled plasma intended for clinical applications.
ADVANTAGE - Binding the virus to a receptor improves the sepn. effect and allows the use of a larger pore diam. in the filter (to increase filtration rate) while still ensuring removal of even small viruses such as picorna and parvo viruses. Larger protein mols., e.g. **factor VIII** or non Willebrand **factor**, are retained in soln.
Dwg.0/0
FS CPI
FA AB
MC CPI: B04-B04D4; B04-G01; B11-B; D05-H06; D05-H13

L39 ANSWER 6 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1996-105860 [11] WPIX
CR 1997-145210 [13]
DNN N1996-088669 DNC C1996-033519
TI High purity fibrinogen concentrate free of viral contamination - useful in pharmaceuticals and cosmetics, also new appts. including system for viral inactivation by exposure to ultra-violet C light.
DC B04 D21 D22 P34
IN DE WAEL, L; LAUB, R; WAEL, L D
PA (CROI-N) CROIX-ROUGE BELGIQUE; (CAFD-N) CAF-DCF DEPT CENT FRACTIONNEMENT CROIX R
CYC 15
PI WO 9602571 A1 19960201 (199611)* FR 34p C07K014-75 <--
RW: AT BE CH DE DK ES FR GB IT LI NL SE
W: CA JP US
EP 771324 A1 19970507 (199723) FR C07K014-75 <--
R: AT BE CH DE DK ES FR GB IT LI NL SE
JP 10506607 W 19980630 (199836) 31p C07K014-75
US 5834420 A 19981110 (199901) A61K035-14
EP 771324 B1 19990922 (199943) FR C07K014-75
R: AT BE CH DE DK ES FR GB IT LI NL SE
DE 69512416 E 19991028 (199951) C07K014-75
ES 2139227 T3 20000201 (200013) C07K014-75
ADT WO 9602571 A1 **WO 1995-BE69 19950714**; EP 771324 A1 **EP 1995-927599 19950714, WO 1995-BE69 19950714**; JP 10506607 W **WO 1995-BE69 19950714, JP 1996-503538 19950714**; US 5834420 A **WO 1995-BE69 19950714, US 1997-765838 19970707** ; EP 771324 B1 **EP 1995-927599 19950714, WO 1995-BE69 19950714**; DE 69512416 E **DE 1995-612416 19950714, EP 1995-927599 19950714, WO 1995-BE69 19950714**; ES 2139227 T3 **EP 1995-927599 19950714**
FDT EP 771324 A1 Based on WO 9602571; JP 10506607 W Based on WO 9602571; US 5834420 A Based on WO 9602571; EP 771324 B1 Based on WO 9602571; DE

69512416 E Based on EP 771324, Based on WO 9602571; ES 2139227 T3 Based on EP 771324

PRAI **EP 1994-870121 19940714**

REP DE 3001435; EP 131740; EP 18561; EP 311950; EP 555135; WO 8605190; WO 8912065; WO 9305067

IC ICM A61K035-14; C07K014-75
ICS A61K038-16; A61K038-36; A61L002-18; C07K001-00; C07K001-18; **C07K001-34**; C07K001-36; C07K014-00; C07K017-00

AB WO 9602571 A UPAB: 20000313
Fibrinogen concentrate (A) is free of viral contaminants and has purity >95%.

Also claimed are a biological glue contg. (A) and the appts. for preparing (A).

USE - (A) is useful in pharmaceutical and cosmetic formulations (claimed) e.g. for healing wounds, as **coagulants** and for treating fibrinogenaemia.

ADVANTAGE - (A) is very pure (pref. >98%) and uncontaminated by viruses, lipids or proteases (claimed). It also includes some **factor VIII**, making it useful in biological glues. (A) can be produced by a simple, rapid and inexpensive method which is suitable for large scale use, partic. as it involves few, if any, chromatography stages.

Dwg.0/6

FS CPI GMPI

FA AB

MC CPI: **B04-H19**; B11-C09; B14-F08; B14-N17B; D08-B; D09-C

L39 ANSWER 7 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1996-068830 [07] WPIX

DNC C1996-022418

TI Filtering macromolecule soln. with specific salt content - to remove virus e.g. hepatitis A, polio and HIV viruses.

DC B04

IN WINGE, S

PA (PHAA) PHARMACIA AB

provided

CYC 25

PI	WO 9600237	A1 19960104 (199607)* EN	39p	C07K001-34	<--
	RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE				
	W: AU CA FI JP MX NO NZ US				
	SE 502820	C2 19960122 (199609)		C07K001-34	<--
	AU 9528132	A 19960119 (199616)		C07K001-34	<--
	FI 9605145	A 19961220 (199713)		C07K000-00	<--
	NO 9605523	A 19961220 (199713)		C07K001-34	<--
	EP 796269	A1 19970924 (199743) EN		C07K001-34	<--
	R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE				
	ES 2105992	T1 19971101 (199750)		C07K001-34	<--
	AU 682274	B 19970925 (199802)		C07K001-34	<--
	NZ 288789	A 19971219 (199807)		B01D061-14	<--
	JP 10502074	W 19980224 (199818)	39p	C07K001-34	<--
	MX 9606639	A1 19970301 (199820)		C07K001-34	<--

ADT WO 9600237 A1 **WO 1995-SE777 19950622**; SE 502820 C2 **SE 1994-2254 19940623**; AU 9528132 A **AU 1995-28132 19950622**; FI 9605145 A **WO 1995-SE777 19950622, FI 1996-5145 19961220** ; NO 9605523 A **WO 1995-SE777 19950622, NO 1996-5523 19961220**; EP 796269 A1 **EP 1995-923651 19950622, WO 1995-SE777 19950622**; ES 2105992 T1 **EP 1995-923651 19950622**; AU 682274 B **AU 1995-28132 19950622**; NZ 288789 A **NZ 1995-288789 19950622, WO 1995-SE777 19950622**; JP 10502074 W **WO 1995-SE777 19950622, JP 1996-503062 19950622**; MX 9606639 A1 **MX 1996-6639 19961218**

FDT AU 9528132 A Based on WO 9600237; EP 796269 A1 Based on WO 9600237; ES 2105992 T1 Based on EP 796269; AU 682274 B Previous Publ. AU 9528132, Based on WO 9600237; NZ 288789 A Based on WO 9600237; JP 10502074 W Based on WO 9600237

PRAI **SE 1995-724 19950224; SE 1994-2254 19940623**

REP 1.Jnl.Ref; EP 219295; EP 307373

IC ICM B01D061-14; C07K000-00; **C07K001-34**
ICS C07K014-765; C07K014-81
ICA C07K007-02
AB WO 9600237 A UPAB: 19960222
Virus filtering a soln. contg. at least one macromolecule where the total salt content of the soln. is 0.2M upto the satn. of the soln. is claimed.
The total salt content of the soln. is pref. 0.4-2.5 (pref. 0.6-2.0) M and the salt is NaCl, KCl, NaOAc and/or sodium citrate. The macromolecule is a protein, polysaccharide and/or polypeptide esp. **Factor** IX, gammaglobulin, albumin, antithrombin III, or a deletion deriv. of recombinant **factor VIII**. The method is carried out in accordance with the 'dead'end' filtering technique and the process reduces the content of non-enveloped viruses by 4 logs.
USE - The method can be used on different types of macromolecule solns. primarily contg. proteins and to remove different types of virus. Undesirable proteins can be sepd. from the prod.. It reduces the content of virus with or without lipid envelopes e.g. hepatitis A, polio, parvo, hepatitis B, hepatitis C and HIV viruses.
ADVANTAGE - The residence time is reduced and the liq. volumes used can be reduced as well as the filter area. The macromolecule yield is > 90% and polymsn. is reduced on the virus filter surface, to enable the rate of flow to be increased and the process time to be decreased.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-F11; B11-B

L39 ANSWER 8 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1995-180333 [24] WPIX
DNC C1995-083526
TI Prepn. of an anti-haemophilic factor from a cryo-precipitate - comprises virus inactivation steps involving heat treatment followed by a solvent-detergent process.
DC B04
IN WOLTER, D
PA (BLUT-N) BLUTSPENDEDIENST DRK-LANDESVERBAENDE
CYC 1
PI DE 4431833 C1 19950518 (199524)* 3p C07K001-36 <--
ADT DE 4431833 C1 **DE 1994-4431833 19940907**
PRAI **DE 1994-4431833 19940907**
IC ICM C07K001-36
ICS A61K035-16
AB DE 4431833 C UPAB: 19950626
The prepn. of a concentrate of AHF (antihaemophilic **factor-Factor VIII**) from a cryoppte. comprises: (a) suspending and dissolving the cryoppte.; (b) removing non-AHF proteins and precipitating AHF in a known manner to give a crude AHF paste as a sediment; (c) carrying out a first virus inactivation of the crude AHF paste by heat treatment in the presence of 0.7-1.4 g/ml calcium gluconate and 1.25-1.5 g/ml sucrose pooled concentrate and 0.5 mol/l of other protein-stabilising substances chosen from the amino acids glycine, alpha or beta alanine, lysine, leucine, valine, asparagine, serine, hydroxyproline, proline, glutamine, alpha or beta or theta-aminobutyric acid; (d) cooling and diluting with distilled water; (e) carrying out a second virus inactivation using a solvent-detergent (SD) process; (f) purifying the extract by chromatography using a weakly basic anion exchange resin; and (g) ultra **filtering** and diaconcentrating the extract.
ADVANTAGE - The two stage virus inactivation gives total virus inactivation and still achieves high yields of AHF.
Dwg.0/0
FS CPI
FA AB
MC CPI: B04-B04D4; B14-F08

L39 ANSWER 9 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1993-102899 [13] WPIX
DNC C1993-045372
TI High yield purificn. of **factor VIII** from cryo-ppte. - by treating with alumina gel, viral inactivation and chromatography on hydrophilic weak anion exchanger.
DC B04
IN GRANDGEORGE, M; LUTSCH, C
PA (INMR) PASTEUR MERIEUX SERUMS & VACCINS
CYC 21
PI EP 534812 A1 19930331 (199313)* FR 7p C07K003-22 <--
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE
AU 9222168 A 19930401 (199320) C07K003-02 <--
CA 2077888 A 19930327 (199323) C12N009-64 <--
FR 2681867 A1 19930402 (199326) 14p C07K003-22 <--
JP 05279396 A 19931026 (199347) 5p C07K015-06 <--
AU 652660 B 19940901 (199436) C07K003-02 <--
US 5371195 A 19941206 (199503) 4p A61K035-16 <--
ADT EP 534812 A1 **EP 1992-402378 19920901**; AU 9222168 A **AU 1992-22168 19920904**; CA 2077888 A **CA 1992-2077888 19920909**; FR 2681867 A1 **FR 1991-11849 19910926**; JP 05279396 A **JP 1992-282450 19920928**; AU 652660 B **AU 1992-22168 19920904**; US 5371195 A **US 1992-948395 19920923**
FDT AU 652660 B Previous Publ. AU 9222168
PRAI **FR 1991-11849 19910926**
REP EP 367840
IC ICM A61K035-16; C07K003-02; C07K003-22; C07K015-06; C12N009-64
ICS A61K037-547; C07G007-00; C07K003-28; C07K013-00
AB EP 534812 A UPAB: 19930924
Purificn. of **factor VIII** from cryoprecipitate, which has been dissolved and treated conventionally with alumina gel, comprises: (1) diluting the extract to protein concn. 5 g/l or less (pref. 4 g/l) then inactivating virus by solvent/detergent treatment; (2) subjecting the inactivated extract to chromatography on a hydrophilic, weak anion exchanger, and (3) eluting **factor 8** with a dissociating buffer.

Also new is a **factor 8** product prepd. by this method with activity at leat 100 IV **factor 8**:C per mg of protein before the opt. addn. of a stabiliser such as human albumin. Pref. the eluted **factor 8** is subsequently ultra-**filtered, filtered** sterile and freeze-dried.

USE/ADVANTAGE - Provides chromatographic yields of over 90%; avoids the problems (in existing procedures) of possible denaturation by pasteurisation, high sugar concns. and presence of detergent in the product, and does not require buffers contg. glycine and lysine.
0/0
FS CPI
FA AB
MC CPI: **B04-B04D3**; B11-B
ABEQ FR 2681867 A UPAB: 19931116
Purificn. of **factor VIII** from cryoprecipitate, which has been dissolved and treated conventionally with alumina gel, comprises: (1) diluting the extract to protein concn. 5 g/l or less (pref. 4 g/l) then inactivating virus by solvent/detergent treatment; (2) subjecting the inactivated extract to chromatography on a hydrophilic, weak anion exchanger, and (3) eluting **factor 8** with a dissociating buffer.

Also new is a **factor 8** prod. prepd. by this method with activity at least 100 IV **factor 8**:C per mg of protein before the opt. addn. of a stabiliser such as human albumin. Pref. the eluted **factor 8** is subsequently ultra-**filtered, filtered** sterile and freeze-dried.

USE/ADVANTAGE - Provides chromatographic yields of over 90%; avoids the problems (in existing procedures) of possible denaturation by pasteurisation, high sugar concns. and presence of detergent in the product, and does not require buffers contg. glycine and lysine.
Dwg. 0/0

ABEQ US 5371195 A UPAB: 19950126
Purificn. of **factor VIII** from cryoprecipitate comprises dissolving the cryoprecipitate, adding alumina gel, sepg. purified cryoprecipitate extract from the treated soln. diluting to a protein concn. of up to 5g/l and inactivating virus with solvent/detergent, performing chromatography with a weak anion exchange column which is hydrophilic in nature, and eluting **factor VIII** with a dissociating buffer.
ADVANTAGE - Yields of over 90% are achieved. Avoids the risks of denaturation by pasteurisation, use of high sugar concns. presence of Tween 80 in the eluted product or the use of buffer contg. Gly and Lys. Dwg.0/0

L39 ANSWER 10 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1991-369187 [50] WPIX
DNC C1991-159142
TI Isolation of high-purity factor VIII - by immuno-sorption after adding divalent ions.
DC A96 B04 D16
IN **CHTOUROU, A**
PA (NATR-N) FONDATION NAT TRANS
CYC 15
PI WO 9118017 A 19911128 (199150)*
RW: AT BE CH DE DK ES FR GB GR IT LU NL SE
W: CA US
FR 2662166 A 19911122 (199206)
ADT FR 2662166 A FR 1990-6252 19900518
PRAI FR 1990-6252 19900518
REP EP 123945; EP 152746; EP 286323
IC **A61K035-16; A61K037-47**; C07K003-18; C07K013-00
AB WO 9118017 A UPAB: 19930928
Isolation of high-purity factor VIII (FVIII) from aq. mixts. contg. FVIII complexed with von Willebrand factor (vWF) is effected by (a) adding sufficient divalent ions to dissociate the FVIII-vWF complex, (b) contacting the mixt. with an immunosorbent comprising an anti-FVIII monoclonal antibody covalently immobilised on a rigid support, and (c) eluting FVIII from the immunosorbent. The antibody is directed against the light chain of FVIII, is capable of inhibiting the coagulant activity of FVIII:C, and is capable of binding to FVIII by strong hydrophobic interactions.
The starting material is plasma, solubilised cryoprecipitate, a prepurified FVIII concentrate, or a culture supernatant contg. recombinant FVIII. The divalent ions (esp. Ca2+) are added in a concn. of 0.1-0.6 (esp. 0.2-0.4)M. The antibody is 463A8 (Thrombosis and Haemostasis, 56/3), 271, 1986) and is immobilised on a high-porosity polyacrylamide gel in an amt. of 0.1-5 (esp. 0.3-1) mg/ml. The contact time in step (b) is less than 90 (esp. less than 60) min. when the FVIII/antibody ratio is 200-600 IU/mg. Elution is effected with a buffer soln. contg. a detergent. The eluate may be further purified by ion-exchange chromatography.
ADVANTAGE - Step (a) accelerates the immunosorption of FVIII in step (b) and increases the yield of purified FVIII (cf. EP286323).
0/4
FS CPI
FA AB
MC CPI: A12-V03C2; A12-W11L; B04-B04D3; D05-H13

L39 ANSWER 11 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1991-295372 [40] WPIX
DNC C1991-127660
TI Prepn. of factor VIII soln. of intermediate purity - starting from cryo-ppte. by solubilising, adding polysaccharide sulphate to ppte. fibrinogen and fibronectin, filtering, re-pptn. etc..
DC B04
IN **CHTOUROU, A**
PA (NATR-N) FOND NAT TRANSFUS S; (NATR-N) FONDATION NAT TRANS
CYC 15

PI WO 9113625 A 19910919 (199140)*
RW: AT BE CH DE DK ES FR GB GR IT LU NL SE
W: US
FR 2659557 A 19910920 (199148)
EP 472711 A 19920304 (199210)
R: AT BE CH DE ES FR GB IT LI LU NL SE
FR 2665364 A 19920207 (199215)
ADT FR 2659557 A FR 1990-3328 19900315; EP 472711 A EP 1991-906628 19910315;
FR 2665364 A FR 1990-9828 19900801
PRAI FR 1990-3328 19900315; FR 1990-9828 19900801
REP EP 127603; EP 238701; EP 343275
IC **A61K035-16; A61K037-47**
AB WO 9113625 A UPAB: 19930928
A conc. soln. of Factor VIII, of intermediate purity, is prepd. from a cryo-pptd. by: (a) the cryoprecipitate is solubilised; (b) a polysaccharide sulphate (PSS) is added to the solution under conditions of temp. and concn. such that there is not pptn. of Factor VIII but fibrinogen and fibronectin are pptd.; (c) solid is removed from the supernatant liquid; (d) the liquid is submitted to a second pptn. by the addition of aluminium hydroxide gel. This pptes. vitamin K factors and other proteic contaminants, while leaving the Factor VIII in solution; (e) solid is removed from the supernatant liquid; and (f) liq. is the desired solution of Factor VIII.
USE/ADVANTAGE - Factor VIII is used in the treatment of haemophiliacs. The process is simple and gives a product that may either be used without further purifcn. or is suitable for further purifcn., e.g. by ion exchange chromatography or by gel filtration. @(16pp Dwg.No.0/2)
FS CPI
FA AB
MC CPI: B04-B04D3; B12-H04

L39 ANSWER 12 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1991-178061 [24] WPIX
DNC C1991-076871
TI Isolating **factor 8** in high yield - by gel **filtration** of blood plasma without cryo-precipitation.
DC B04
IN KAERSGAARD, P
PA (NOVO) NOVO-NORDISK AS
CYC 42

PI	WO 9107438	A	19910530 (199124)*		22p		<--
	RW: AT BE CH DE DK ES FR GB GR IT LU NL OA SE						
	W: AU BB BG BR CA DE FI HU JP KP KR LK MC MG MW NO RO SD SU						
	ZA 9008599	A	19910731 (199136)				<--
	AU 9067470	A	19910613 (199137)				<--
	DK 8905621	A	19910510 (199142)				<--
	PT 95830	A	19910930 (199142)				<--
	CN 1051732	A	19910529 (199208)				<--
	FI 9202105	A	19920508 (199232)			C07K	<--
	NO 9201839	A	19920708 (199241)			A61K035-16	<--
	HU 60511	T	19920928 (199245)			C07K015-06	<--
	EP 524172	A1	19930127 (199304)	EN	22p	C07K015-06	<--
	R: AT BE CH DE ES FR GB GR IT LI LU NL SE						
	JP 05501557	W	19930325 (199317)		8p	C07K015-06	<--
	US 5245014	A	19930914 (199338)		9p	C07K003-12	<--
	EP 524172	B1	19950215 (199511)	EN	13p	C07K014-755	<--
	R: AT BE CH DE ES FR GB GR IT LI LU NL SE						
	DE 69017050	E	19950323 (199517)			C07K014-755	<--
	ES 2068404	T3	19950416 (199522)			C07K014-755	<--
	IL 96277	A	19950731 (199540)			C07K001-16	<--
	IE 66836	B	19960207 (199615)			C07K015-02	<--
	CA 2073012	C	19960319 (199622)			C07K014-755	<--
	JP 2509407	B2	19960619 (199629)		9p	C07K014-755	<--
	RU 2055593	C1	19960310 (199649)		12p	A61K039-04	<--
	NO 180741	B	19970303 (199716)			A61K035-16	<--
	SK 278640	B6	19971210 (199811)			A61K035-16	<--

SK 9005371	A3 19971210 (199811)	A61K035-16	<--
CZ 9005371	A3 19980513 (199825)	C07K014-755	<--
HU 214905	B 19980728 (199842)	C07K014-755	<--
FI 103510	B1 19990715 (199934)	C07K001-14	

ADT ZA 9008599 A **ZA 1990-8599 19901026**; FI 9202105 A **WO 1990-DK279 19901105, FI 1992-2105 19920508**; NO 9201839 A **WO 1990-DK279 19901105, NO 1992-1839 19920508**; HU 60511 T **WO 1990-DK279 19901105, HU 1992-1551 19901105**; EP 524172 A1 **EP 1990-917201 19901105, WO 1990-DK279 19901105**; JP 05501557 W **WO 1990-DK279 19901105, JP 1991-500067 19901105**; US 5245014 A **US 1990-610480 19901107**; EP 524172 B1 **EP 1990-917201 19901105, WO 1990-DK279 19901105**; DE 69017050 E **DE 1990-617050 19901105, EP 1990-917201 19901105, WO 1990-DK279 19901105**; ES 2068404 T3 **EP 1990-917201 19901105**; IL 96277 A **IL 1990-96277 19901108** ; IE 66836 B **IE 1990-4022 19901108**; CA 2073012 C **CA 1990-2073012 19901105**; JP 2509407 B2 **WO 1990-DK279 19901105 , JP 1991-500067 19901105**; RU 2055593 C1 **SU 1990-5052211 19901105, WO 1990-DK279 19901105**; NO 180741 B **WO 1990-DK279 19901105, NO 1992-1839 19920508**; SK 278640 B6 **CS 1990-5371 19901101**; SK 9005371 A3 **CS 1990-5371 19901101** ; CZ 9005371 A3 **CS 1990-5371 19901101**; HU 214905 B **WO 1990-DK279 19901105, HU 1992-1551 19901105**; FI 103510 B1 **FI 1992-2105 19920508**

FDT HU 60511 T Based on WO 9107438; EP 524172 A1 Based on WO 9107438; JP 05501557 W Based on WO 9107438; EP 524172 B1 Based on WO 9107438; DE 69017050 E Based on EP 524172, Based on WO 9107438; ES 2068404 T3 Based on EP 524172; JP 2509407 B2 Previous Publ. JP 05501557, Based on WO 9107438; NO 180741 B Previous Publ. NO 9201839; SK 278640 B6 Previous Publ. SK 9005371; HU 214905 B Previous Publ. HU 60511, Based on WO 9107438; FI 103510 B1 Previous Publ. FI 9202105

PRAI **DK 1989-5621 19891109**

REP 1.Jnl.Ref; EP 104356; EP 321835; EP 399321; US 4675385; WO 8909784

IC ICM A61K035-16; A61K039-04; C07K001-14; C07K001-16; C07K003-12; **C07K014-755**; C07K015-02; C07K015-06; C07K033-48
ICS A61K037-02; A61K037-54; A61K037-547; A61K038-037; **A61K038-37** ; C12N009-50

AB WO 9107438 A UPAB: 19930928
A method for isolating **Factor 8** from other blood plasma proteins using a gel **filtration** medium is claimed. Blood plasma is subjected to gel **filtration** under group sepn. conditions using a high load and high flow rate. The medium contains particles inert to **Factor 8** which have a fractionation range of 1x10power-3 - 1x10power-**8**.

The gel material pref. has a fractionation range of 1x10power-4 - 8x10power-7, pref. 5x10power-4 - 4x10power-7. The vol. of plasma added is at least 5%, pref. 15-40% of the bed vol.. The flow rate is at least 0.3, pref. 0.5-2 bed vols. per hour.

USE/ADVANTAGE - **Factor 8** is produced in a very high yield (above 70%) directly from plasma via a gentle method not involving initial cryoprecipitation The prods. have a specific activity of 1-4 IU **factor 8** coagulation activity/mg.

0/2

FS CPI

FA AB

MC CPI: **B04-B04D3**; B11-B

ABEQ JP 05501557 W UPAB: 19931025
To isolate **Factor 8** from other **blood** plasma proteins using a gel **filtration** medium involves subjecting **blood** plasma to gel **filtration** under group sepn. conditions using a high load and high flow rate. The medium contains particles inert to **Factor 8** which have a fractionation range of 1x10 power(-3) to 1x10 power(-**8**).

The gel material pref. has a fractionation range of 1x10 power(-4) to 8x10 power(-7), (pref. 5x10 power(-4) to 4x10 power(-7). The vol. of plasma added is at least 5% (pref. 15-40%) of the bed vol.. The flow rate

is at least 0.3 (pref. 0.5-2) bed vols. per hour.
USE/ADVANTAGE - **Factor 8** is produced in a very high yield (above 70%) directly from plasma via a gentle method not involving initial cryo-precipitation. The prods. have a specific activity of 1-4 IU **factor 8 coagulation** activity/mg.

ABEQ US 5245014 A UPAB: 19931123
Isolating **factor VIII** from **blood** plasma comprises (i) opt. pretreating **blood** plasma and (ii) subjecting the plasma to gel **filtration** column chromatography under gp. separation conditions. The volume of **blood** plasma added to the column is at least 5% of the bed volume and the flow rate is at least 0.3 bed volumes per hr.. The gel **filtration** medium is inert to **factor VIII** and has a mol.wt. fractionation range of 1 x 10 power 4 to **8** x 10 power 7.
The gel **filtration** medium is pref. a cross linked agarose gel, a mixt. of agarose and acrylic polymer, a copolymer of oligoethyleneglycol, glycidyl methacrylate and pentaerythritol or cellulose gel. The **factor VIII** is further purified by **ultrafiltration**, pptn., ion exchange or affinity chromatography.
USE - **Factor VIII** is an antihaemophilic cpd. that participates in **blood coagulation**.
Dwg.0/2

ABEQ EP 524172 B UPAB: 19950322
A method for isolating **Factor VIII** from other proteins in **blood** plasma using a gel **filtration** medium, characterised in that isolated plasma or thawed freshly frozen plasma which optionally has been pretreated, as long as any optional pretreatment does not have any significant influence on the contents of **Factor VIII** of the plasma, is subjected directly to gel **filtration** under group separation conditions wherein he volume of plasma added is at least 5% of the bed volume and wherein the flow rate is at least 0.3 bed volumes per hour, the gel **filtration** medium being constituted of particles being inert tto **Factor VIII** and having a fractionation range in the interval from 1x103 to 1x108, and the **factor VIII**-main fraction is collected.
Dwg.0/2

L39 ANSWER 13 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1990-356002 [48] WPIX
DNC C1990-154608
TI Prodn. of highly purified anti haemophilic factor - by PEG precipitation gel **filtration** and heat-treating virus inactivation steps.
DC A96 B04 D16
IN BOCKSKOPF, B; BROCKWAY, W; GOELKER, C; SENG, R L
PA (MILE) MILES INC; (FARB) BAYER CORP; (GOEL-I) GOELKER C; (MILE) MILES LAB INC
CYC 17

PI	EP 399321	A	19901128 (199048)*	10p		<--
	R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
	AU 9055868	A	19901129 (199104)			<--
	CA 2017039	A	19901124 (199107)			<--
	JP 03047199	A	19910228 (199115)			<--
	AU 635535	B	19930325 (199319)		C07K003-02	<--
	EP 399321	B1	19930623 (199325) EN	12p	A61K035-16	<--
	R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE					
	DE 69002033	E	19930729 (199331)		A61K035-16	<--
	ES 2042138	T3	19931201 (199401)		A61K035-16	<--
	JP 2931630	B2	19990809 (199937)	11p	C07K014-755	<--
	CA 2017039	C	19990803 (199951) EN		C07K014-755	<--

ADT EP 399321 A **EP 1990-108993 19900512**; JP 03047199 A **JP 1990-133691 19900523**; AU 635535 B **AU 1990-55868 19900523**; EP 399321 B1 **EP 1990-108993 19900512**; DE 69002033 E **DE 1990-602033 19900512, EP 1990-108993 19900512**; ES 2042138 T3 **EP 1990-108993 19900512**; JP 2931630 B2 **JP 1990-133691 19900523**; CA 2017039 C **CA 1990-2017039 19900517**

FDT AU 635535 B Previous Publ. AU 9055868; DE 69002033 E Based on EP 399321; ES 2042138 T3 Based on EP 399321; JP 2931630 B2 Previous Publ. JP 03047199
PRAI **US 1989-356315 19890524**
REP 1.Jnl.Ref; A3...9129; EP 47216; JP 58074617; NoSR.Pub; US 3631018; US 4069216; US 4170639; US 4305871; US 4387092; US 4543210; US 4650858; WO 8400757
IC A61K035-16; C07K003-02; C07K015-06; C12N009-48
ICM A61K035-16; C07K003-02; **C07K014-755**
ICS **A61K038-37**; C07K001-16; C07K001-30; C07K001-36; C07K003-12; C07K003-20; C07K015-06; C12N007-04; C12N009-48
AB EP 399321 A UPAB: 19930928
Prodn. of a concentrate of antihaemophilic **factor** (AHF) from cryoprecipitate comprises: (1) dissolving the cryoprecipitate, (b) removing non-AHF proteins by precipitation with polyethylene glycol (PEG), (c) heat treating the AHF for viral inactivation, then (d) passing the AHF through a gel **filtration** column contg. a size exclusion resin to remove the chemical and to concentrate the AHF to at least 35 units of **Factor VIII** activity per ml. of pooled concentrate.
Prodn. of AHF concentrate comprises: (a) preparing a cryoprecipitate, (b) removing non-AHF proteins by precipitation to form a solubilised AHF pool, (c) passing the pool through a gel **filtration** column, and (d) heating AHF obtd. in a soln. in the presence of sucrose.
USE/ADVANTAGE - The process is used to prepare AHF from human plasma. AHF is known to consist of several components, the component which is active in treating haemophilia A being **Factor VIII**:C. The process gives high yields of highly purified AHF free from infectious agents without loss of therapeutic or immunological activity by mild process steps.
0/1
FS CPI
FA AB
MC CPI: A05-H03; A12-V; A12-W11L; **B04-B04D3**; B11-B; B12-H04; D05-C12; D05-H13
ABEQ EP 399321 B UPAB: 19931116
A process for the production of a concentrte of antihemophilic **factor** (AGF) from cryoprecipitate without substanital loss of therapeutic or immunological activity comprising the sequential steps of: (a) dissolving said cryoprecipitate; (b) removing non-AHF proteins by precipitation with polethylene glycol (PEG) without a chill step; (c) heat treating said AHF for viral inactivation in the presence of sucrose, the amount of sucrose being 1.2 to 0.6 g/ml of pooled concentrate; and then (d) passing said AHF through a gel **filtration** column containing a size exclusion resin from 300 to 15,000 daltons to concentrte said AHF to at least 35 units of **Factor VIII** activity per ml of pooled concentrate.
Dwg. 0/1

L39 ANSWER 14 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1990-352834 [47] WPIX
DNC C1990-153409
TI Prepn. of blood coagulant **factor 8** - comprises gel **filtration** of aq. soln. contg. the coagulant using insoluble porous gel.
DC B04
PA (GREC) GREEN CROSS CORP
CYC 1
PI JP 02255698 A 19901016 (199047)* 5p <--
JP 2931319 B2 19990809 (199937) 5p C07K014-755 <--
ADT JP 02255698 A **JP 1989-79243 19890329**; JP 2931319 B2 **JP 1989-79243 19890329**
FDT JP 2931319 B2 Previous Publ. JP 02255698
PRAI **JP 1989-79243 19890329**
IC A61K037-46; C07K003-18; C07K013-00
ICM **C07K014-755**
ICS A61K037-46; A61K038-00; **C07K001-34**; C07K003-18; C07K013-00
AB JP 02255698 A UPAB: 19930928

Blood coagulant factor VIII is obtd. by gel **filtration** of aq. soln. contg. **blood coagulant factor VIII** using water insoluble porous gel of which exclusion max. molecular weight is 800,000-100,000,000.

Creo precipitate obtained by freeze-fusion of human **blood** plasma was extracted 5 times with 20 mM tris-10 mM citric acid buffer (pH 7.0) and Al hydroxide gel (1/10 vol. of Creo precipitate) was added and stirred for 30 min. Then bentonite (6 g/l) was added, stirred for 1 hour and centrifuged for 30 min. at the rate of 4,000 r.p.m. to obtain supernatant, which was treated by surfactant (0.3% Tri-n-butylphosphate, 1% Tween 80, 30 deg.C, 6 hours). To the soln. was added glycine (150 g/l) and stirred at 30 deg.C for 1 hour followed by centrifuging (4,000 r.p.m. 30 deg.C, 30 min.=. Na chloride (87 g/l) was added to the supernatant and the mixture was stirred for 1 hour followed by centrifuging. The precipitate was further purified by gel **filtration** using Sephacryl S-400 HR column (Pharmacia) to give **blood coagulant factor VIII.**

USE/ADVANTAGE - The new method is very useful because it can efficiently give **blood coagulant factor VIII** which is highly soluble and contains little impure protein.

0/0

FS CPI
FA AB
MC CPI: **B04-B04D3;** B12-H04

L39 ANSWER 15 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1990-148994 [20] WPIX
DNC C1990-065174
TI Highly pure non-infectious anti haemophilia factor prepn. - using blood plasma fraction which has been enriched with the factor using chromatographic method.
DC A96 B04
IN SMITH, A
PA (OCTA-N) OCTAPHARMA AG
CYC 13
PI EP 367840 A 19900516 (199020)* <--
R: AT CH DE ES FR GB IT LI NL SE
WO 9005140 A 19900517 (199023) <--
W: DK FI JP
FI 9003366 A 19900704 (199040) <--
DK 9001615 A 19900704 (199045) <--
JP 03502200 W 19910523 (199127) <--
EP 367840 B1 19930203 (199305) DE 6p A61K035-16 <--
R: AT CH DE ES FR GB IT LI NL SE
DE 3878245 G 19930318 (199312) A61K035-16 <--
ES 2053684 T3 19940801 (199432) A61K035-16 <--
ADT EP 367840 A **EP 1988-118478 19881105;** JP 03502200 W **JP 1989-500028 19891019;** EP 367840 B1 **EP 1988-118478 19881105;** DE 3878245 G **DE 1988-3878245 19881105, EP 1988-118478 19881105;** ES 2053684 T3 **EP 1988-118478 19881105**
FDT DE 3878245 G Based on EP 367840; ES 2053684 T3 Based on EP 367840
PRAI **EP 1988-118478 19881105**
REP DE 2715832; EP 104356; EP 173242; GB 1178958; US 4386068; WO 8604486; 1.Jnl.Ref; DE 2635894; EP 144957; EP 238701; EP 239859; EP 245875; EP 343275
IC ICM A61K035-16
ICS C07K003-22; C07K015-06
AB EP 367840 A UPAB: 19930928
The prepn. of a highly pure, non-infectious anti-haemophilia **factor** (AHF or **factor VIII**) from **blood** plasma comprises treating a **blood** plasma fraction which has been enriched with **factor VIII** using a chromatographic method with biocompatible organic solvents/detergents and then subjecting the fraction to further purificn. processes.

Pref. the **blood** plasma fraction has been obtd. by gel

permeation chromatography using an ion exchanger, which is esp. an anionic exchange resin such as DEAE-modified material. Pref. the **factor VIII** contg. fraction is mixed with an aluminium hydroxide suspension and then, after cooling to 10-18 deg.C is centrifuged or **filtered**. Pref. the purificn. work up steps are also by chromatography, esp. gel permeation chromatography using an anion exchange material such as a DEAE-modified material.

USE/ADVANTAGE - **Factor VIII** can be obtd. in high yields for the first time in a highly pure condition, and has a specific activity not previously achieved. The previously necessary steps of ethanol pptn. or cryopptn. which were previously necessary, and which destroy a proportion of the **factor VIII** are avoided.

0/0

FS CPI
FA AB
MC CPI: A12-V; **B04-B04D3**
ABEQ EP 367840 B UPAB: 19930928

A process for the preparation of a highly pure non-infectious antihaemophilic **factor** (AHF or **factor VIII**) from **blood** plasma by treating a fraction wherein the **factor VIII** has been accumulated with biologically compatible organic solvents/detergents, followed by further purification steps, characterised in that the fraction wherein the **factor VIII** has been accumulated is recovered by means of a chromatographic separation on a hydrophilic chromatography material based on copolymers of oligoethyleneglycols, glycidyl methacrylates and pentaerythrol dimethacrylates, the chromatography material having been modified with ion exchanger groups.

0/0

L39 ANSWER 16 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1989-173765 [24] WPIX
DNC C1989-076855
TI Rapid sepn. of pure **factor-8** from plasma - by adsorption on barium citrate, elution, polyether pptn., gel **filtration** and chromatography.
DC A96 B04 J01
IN REUNING, U
PA (SCHE-I) SCHEEFERS H
CYC 1
PI DE 3740520 A 19890608 (198924)* 3p <--
ADT DE 3740520 A **DE 1987-3740520 19871130**
PRAI **DE 1987-3740520 19871130**
IC B01J041-06; C07K003-24; C07K015-06; C07K017-14; C12N011-16
AB DE 3740520 A UPAB: 19930923

High purity **factor 8** is recovered from an aq. soln. by (1) adsorption on Ba nitrate, pptn. and elution; (2) pptn. twice with a polyether; (3) chromatography on an anion exchanger (DEAE material); (4) gel **filtration**; and (5) two sequential h.p. l.c./f.p.l.c. (fast protein liq. chromatography) steps at room temp.

Step (2) is with polyethylene glycol (PEG) added, as a solid to a final concn. of 4wt.-vol.% in the first pptn., and to 35 wt.-vol.% in the second.

The enriched material from step (3) is gel-**filtered**, esp. on 'Superpose' (RTM), and material from this operation is subjected to h.p.l.c./f.p.l.c. (a) on an anion exchanger material esp. 'FPLC-Mono QHR'(RTM), then (b) on a hydrophobic interaction support, esp. 'FPLC-Phenyl-Superpose'(RTM).

USE/ADVANTAGE - To isolate **factor 8** from human or animal plasma, and is quicker then known procedures (only a few hrs. compared with several days).

0/0

FS CPI
FA AB
MC CPI: A05-H03; A12-V03B; A12-W11L; **B04-B04D3**; B11-B; J01-D01A

L39 ANSWER 17 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1988-156669 [23] WPIX
DNC C1988-069841
TI **Factor 8** fraction of high specific activity prodn. - from cryo-ppte. by removing protein impurities, pptn. of **factor 8**, dissolving ppte., lyophilisation and heat inactivation of viruses.
DC B04
IN LINNAU, Y; SCHWARZ, O
PA (IMMO) IMMUNO AG; (IMMO) IMMUNO CHEM MEDIZINISCHE PROD
CYC 17
PI EP 270516 A 19880608 (198823)* DE 8p <--
R: AT BE CH DE ES FR GB IT LI LU NL SE
JP 63132899 A 19880604 (198828) <--
DK 8705735 A 19880504 (198830) <--
US 4814435 A 19890321 (198914) 4p <--
AT 8602923 A 19900615 (199029) <--
EP 270516 B 19910403 (199114) <--
R: AT BE CH DE ES FR GB IT LI LU NL SE
DE 3769096 G 19910508 (199120) <--
CA 1297011 C 19920310 (199216) <--
ES 2028913 T3 19920716 (199234) A61K035-16 <--
JP 07030117 B2 19950405 (199518) 5p C07K014-755 <--
ADT EP 270516 A **EP 1987-890237 19871029**; JP 63132899 A **JP 1987-278985 19871102**; US 4814435 A **US 1987-108458 19871015**; ES 2028913 T3 **EP 1987-890237 19871029**; JP 07030117 B2 **JP 1987-278985 19871102**
FDT ES 2028913 T3 Based on EP 270516; JP 07030117 B2 Based on JP 63132899
PRAI **AT 1986-2923 19861103**
REP A3...8825; AT 379510; EP 127025; EP 127603; EP 159311; No-SR.Pub; WO 8204395; WO 8605190
IC ICM A61K035-16; **C07K014-755**
ICS A61K037-02; A61K038-43; C07K001-30; C07K003-24; C07K015-06; C07K015-14
AB EP 270516 A UPAB: 19930923
Prodn. of **factor 8** contg. fraction with specific activity at least 2.5U/mg protein and immunoglobulin G content at most 10mg/1000U **factor 8** comprises (1) pptg., and removing, unwanted protein from a **factor 8**-contg. plasma fraction in presence of sulphated polysaccharide at neutral pH; (2) treating the purified soln. with a protein pptn. agent (A) to form a **factor 8**-contg. ppte.; (3) dissolving up this ppte. and lyophilising the soln.; and (4) heating the lyophilisate at sufficient temp. and for sufficient time to inactivate viruses.
(A) is (NH4)2SO4 (opt. mixed with glycine or Na citrate); NaCl-glycine; Na2SO4 (opt. mixed with Na citrate) or citrate-glycine.
In step (4), the lyophilisate is adjusted to 5-70, esp. below 40, wt.% moisture content and heated in a closed container at 50-121 deg. C with increasing partial pressure of water vapour, partic. at pressure 0.01-2bar for up to 100 hr.
USE/ADVANTAGE - When used for therapeutic and prophylactic applications, this compsn. has reduced risk of transferring bacterial or viral infections (particularly AIDS and hepatitis). The method provides a compsn. of high specific activity; low IgG content and adequate heat stability.
0/0
FS CPI
FA AB
MC CPI: B02-V02; B04-B04C6; B04-B04D2; B12-A01; B12-A06; B12-G02
ABEQ EP 270516 B UPAB: 19930923
Prodn. of **factor 8** contg. fraction with specific activity at least 2.5U/mg protein and immunoglobulin G content at most 10mg/1000U **factor 8** comprises (1) pptg., and removing, unwanted protein from a **factor 8**-contg. plasma fraction in presence of sulphated polysaccharide at neutral pH; (2) treating the purified soln. with a protein pptn. agent (A) to form a

factor 8-contg. ppte.; (3) dissolving up this ppte. and lyophilising the soln.; and (4) heating the lyophilisate at sufficient temp. and for sufficient time to inactivate viruses.

(A) is (NH4)2SO4 (opt. mixed with glycine or Na citrate); NaCl-glycine; Na2SO4 (opt. mixed with Na citrate) or citrate-glycine.

In step (4), the lyophilisate is adjusted to 5-70, esp. below 40, wt.% moisture content and heated in a closed container at 50-121 deg. C with increasing partial pressure of water vapour, partic. at pressure 0.01-2bar for up to 100 hr.

USE/ADVANTAGE - When used for therapeutic and prophylactic applications, this compsn. has reduced risk of transferring bacterial or viral infections (particularly AIDS and hepatitis). The method provides a compsn. of high specific activity; low IgG content and adequate heat stability.

0/0

ABEQ US 4814435 A UPAB: 19930923

Prodn. of **factor VIII** (AHF) comprises isolation of a crude **factor VIII** fraction; selective pptn. of protein impurities with sulphated polysaccharide at pH 6.0-6.4 and temps. 0-25C; removal of the ppt; then pptn. of the required **factor VIII** protein with (NH4)2SO4, opt. mixed with glycine, NaCl or Na citrate, or similar salt mixts., (8035 wt. %), at pH 5.6-6.**8**; sepn. of the ppt. and dissolution in a buffer soln.; followed by purification by **ultrafiltration**, dialysis and freeze-drying; and heat treatment at 50-121 C in steam to destroy pathogens.

USE - The prods. are propylactics and therapeutics with an activity at least 2.5 int. units/mg protein, and also contain immunoglobulin G (IgG), (up to 10 mg/1000 units **factor VIII**).

L39 ANSWER 18 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1987-272285 [39] WPIX

DNC C1987-115573

TI Prodn. of high-purity **factor VIII** - by sepn. of fibrinogen, globulin(s) and albumin(s) from cryo precipitate.

DC B04 D16

IN SMITH, A

PA (OCTA-N) OCTAPHARMA AG; (LECA-N) LECARSA SA

CYC 11

PI EP 238701 A 19870930 (198739)* DE 7p <--
R: AT BE CH DE FR GB IT LI LU
EP 238701 B 19920318 (199212) 3p <--
R: AT DE FR GB IT NL SE
DE 3684459 G 19920423 (199218) <--

ADT EP 238701 A **EP 1986-104297 19860327**; EP 238701 B **EP 1986-104297 19860327**

PRAI **EP 1986-104297 19860327**

REP AT 349639; FR 2184898; FR 2411608; US 4170639; US 4478825; US 4543210

IC A61K035-16; C07K003-24

AB EP 238701 A UPAB: 19930922

Prodn. of high-purity **factor** (**VIII**) by . of fibrinogen, globulins and albumins from cryoprecipitate is effected by (a) suspending the thawed cryoprecipitate in a 2-fold vol. of H2O contg. 113 U/ml of Na heparin at 10-20 deg. C, (b) adjusting the pH to 7-**8** with dil. HOAc, (c) stirring at 10-20 deg. C while slowly adding an equal vol. of 7-30% aq. EtOH contg. 1-3 U/mol of Na heparin, (d) adjusting the pH to 6.**8**-7.2 with dil. HOAc, (e) slowly cooling to 10-15 deg. C while stirring, (f) sepig. the ppte., and (g) working up the supernatant in known manner.

Step (g) is effected by adding A-(OH)3, centrifuging, **filtering** the supernatant, adding Na cholate/TNBP to inactivate viruses removing the Na cholate/TNBP by oil extraction, and **ultrafiltering** the aq. phase.

ADVANTAGE - The process gives high yields of **factor VIII** with higher purity than commercial prods.

0/0

FS CPI

FA AB
MC CPI: **B04-B04D3**; D05-H13
ABEQ DE 3684459 G UPAB: 19930922
Prodn. of high-purity **factor** (**VIII**) by . of fibrinogen, globulins and albumins from cryoprecipitate is effected by (a) suspending the thawed cryoprecipitate in a 2-fold vol. of H2O contg. 113 U/ml of Na heparin at 10-20 deg. C, (b) adjusting the pH to 7-**8** with dil. HOAc, (c) stirring at 10-20 deg. C while slowly adding an equal vol. of 7-30% aq. EtOH contg. 1-3 U/mol of Na heparin, (d) adjusting the pH to 6.**8**-7.2 with dil. HOAc, (e) slowly cooling to 10-15 deg. C while stirring, (f) sepig. the ppte., and (g) working up the supernatant in known manner.

Step (g) is effected by adding A-(OH)3, centrifuging, **filtering** the supernatant, adding Na cholate/TNBP to inactivate viruses removing the Na cholate/TNBP by oil extraction, and **ultrafiltering** the aq. phase.

ADVANTAGE - The process gives high yields of **factor** **VIII** with higher purity than commercial prods.

ABEQ EP 238701 B UPAB: 19930922
A process for preparing a highly purified anti-hemophilia **factor** (AHF or **factor VIII**) by removing fibrinogen, globulin, and albumin from the cryoprecipitate, characterised in that a) the thawed cryoprecipitate is suspended at 10 to 20 deg.C in about the double volume of water containing from 1 to 3 U/ml of heparin sodium; b) adjusted to pH 7.0 to **8**.0 using dilute acetic acid; c) slowly treated at 10 to 20 deg.C with about the same volume of aqueous ethanol (7 to 30% wt./vol.) containing from 1 to 3 U/ml of heparin sodium; d) adjusted to pH 6. **8** to 7.2 using dilute acetic acid; e) slowly cooled to 10 to 15 deg.C with stirring; f) the precipitate is removed; and g) the supernatant is processed in a per se known manner.

L39 ANSWER 19 OF 19 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1985-307665 [49] WPIX
DNC C1985-132979
TI Cryoprecipitate separation system - to give **Factor-VIII** for treatment of haemophilia.
DC B04 J01
PA (NISS-N) NISSHO CORP
CYC 1
PI JP 60214739 A 19851028 (198549)* 6p <--
JP 03059707 B 19910911 (199140) <--
ADT JP 03059707 B **JP 1984-69531 19840406**
PRAI **JP 1984-69531 19840406**
IC A61K035-16
AB JP 60214739 A UPAB: 19930925
The system is that continuous plasma **filtration** is conducted through a film with the maximum pore size 0.1 to 1.0 micron at a temperature between 6 and 10 deg.C, and sepg. into cryoprecipitate-rich plasma and cryoprecipitate-poor plasma as the **filtrate**. The cryoprecipitate-rich plasma is housed in a vessel kept at 60 deg.C or less.

USE/ADVANTAGE - The system is used to separate the cryoprecipitate contg. a large amount of **blood** clotting **factor** = **VIII** for use in the treatment of haemophilia patients. It separates the cryoprecipitate-rich plasma from the plasma sepd. from whole **blood**. It is excellent in separation efficiency for the cryoprecipitate-rich plasma and separates high quality cryoprecipitate-rich plasma contg. little fibrinogen.
0/0
FS CPI
FA AB
MC CPI: B04-B04D; B11-B; J01-C03; J01-F02B

=> d 10 abs tech

L40 ANSWER 10 OF 11 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1987-356672 [51] WPIX
AB EP 249932 A UPAB: 19930922
Process and appts. for automatic purificn. of a physiologically active substance are claimed.
The process comprises (a) **filtering** a soln. contg. (I) through at least one **filter** with a pore size of 0.22-500 microns; (b) opt. subjecting the **filtrate** to **ultrafiltration** to obtain a concentrate contg. (I) and a permeate contg. impurities with a lower molecular wt. than (I); and (c) subjecting the **filtrate** or concentrate to affinity chromatography to obtain a purified soln. of (I). Also claimed is a carrier with an antibody fixed thereto for recovering a protein from a cell culture soln., where the carrier is sterilised.
USE/ADVANTAGE - The process is esp. useful for recovering proteins from culture solns. of leucocytes, lymphoblasts, hybridomas, E. coli, B. subtilis or yeast, the protein being interferon, urokinase, pro-urokinase, kallikrein, lysozyme, trypsin inhibitor, human granulocyte-differentiation-inducing glycoprotein, interleukin, CSF, tissue plasminogen activator, B-cell growth factor, TNF, epidermal growth factor, lymphotoxin, a hormone, a monoclonal antibody, erythropoietin, antithrombin III, transferrin, plasminogen, plasminogen activator, alpha-fetoprotein or hepatitis B surface antigen. Automation reduces the time and labour required and facilitates maintenance of aseptic conditions.
0/3

=> d all abeq tech tot

L45 ANSWER 1 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-360082 [31] WPIX
DNC C1999-106780
TI Removing viruses from **factor VIII** solution - by **filtration** on nanoporous hydrophilic **filter**.
DC B04
IN **CHTOUROU, A S; NOGRE, M; PORTE, P;**
CHTOUROU, A
PA (FRFR-N) LAB FR DU FRACTIONNEMENT & BIOTECHNOLOGI
CYC 23
PI FR 2772381 A1 19990618 (199931)* 24p C07K001-34 <--
WO 9931138 A1 19990624 (199932) FR C07K014-755 <--
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU CA JP US
AU 9915681 A 19990705 (199948) C07K014-755 <--
EP 1037923 A1 20000927 (200048) FR C07K014-755 <--
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT FR 2772381 A1 **FR 1997-15888 19971215**; WO 9931138 A1 WO 1998-FR2715 19981214; AU 9915681 A AU 1999-15681 19981214; EP 1037923 A1 EP 1998-959975 19981214, WO 1998-FR2715 19981214
FDT AU 9915681 A Based on WO 9931138; EP 1037923 A1 Based on WO 9931138
PRAI **FR 1997-15888 19971215**
IC ICM **C07K001-34; C07K014-755**
ICS **A61K038-37**
AB FR 2772381 A UPAB: 19990806
Process for preparing a virus-safened solution of **factor VIII** (FVIII) containing no high-molecular-weight **von Willebrand factor** (**vWF**) comprises (a) preparing a high-purity FVIII solution containing or not containing high-molecular-weight **vWF**-FVIII complexes, (b) dissociating any high-molecular-weight **vWF**-FVIII complexes in the solution, and (c) **filtering** the solution on a hydrophilic **filter** having a pore size as low as 15 nm.
USE - for treating haemophilia A.
ADVANTAGE - The process removes both high-molecular-weight **vWF** and viruses, including small viruses such as parvovirus B19.

Dwg.0/1
FS CPI
FA AB
MC CPI: **B04-H19**; B14-F08

L45 ANSWER 2 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-113828 [10] WPIX
CR 1990-241997 [32]
DNN N1999-083646 DNC C1999-033564
TI Removal of virus from blood products.
DC B04 J01 P34
PA (ASAH) ASAHI KASEI KOGYO KK
CYC 1
PI JP 10337445 A 19981222 (199910)* 6p B01D061-24
ADT JP 10337445 A **Div ex JP 1988-320349 19881221, JP 1998-131009 19881221**
PRAI **JP 1988-320349 19881221; JP 1998-131009 19881221**
IC ICM B01D061-24
ICS A61K035-14; A61K038-43; A61M001-32
AB JP 10337445 A UPAB: 19990316
Removal of a virus from raw materials of useful protein, particularly blood products, with suspected presence of virus involves using multilayered **filters** having gradient reduced **pore** sizes, particularly a preceding **filter** having **pore** sizes of 50-100 nm and a following **filter** having a **pore** size of at least 30 nm.
ADVANTAGE - The method is used for **filtering** viruses, particularly HBV, from blood products without reduction of biological activities.
Dwg.0/0
FS CPI GMPI
FA AB
MC CPI: B04-B04D5; B04-F11; B04-N02; B11-B; J01-C03

L45 ANSWER 3 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1996-370564 [37] WPIX
CR 1991-117354 [16]; 1992-131461 [16]; 1992-357194 [43]; 1993-196153 [24]; 1993-303199 [38]; 1994-176180 [21]; 1995-130600 [17]; 1995-310843 [40]; 1997-033493 [03]; 1997-064731 [06]; 1997-212052 [19]
DNC C1996-117468
TI Methods of treating blood prods., pref. within 8 hrs. of donation - by centrifuging and **filtering** to separate red cell-contg. sediment layer from platelet-contg. supernatant layer.
DC A23 A96 B04
IN GSELL, T C; MUELLERS, B T; PALL, D B
PA (PALL) PALL CORP
CYC 1
PI US 5543060 A 19960806 (199637)* 13p B01D037-00 <--
ADT US 5543060 A **CIP of US 1989-405977 19890912, Cont of US 1990-609574 19901106, Cont of US 1992-933309 19920821, Cont of US 1994-231914 19940425, US 1995-467322 19950606**
FDT US 5543060 A Cont of US 5152905, Cont of US 5316674, Cont of US 5445736
PRAI **US 1990-609574 19901106; US 1989-405977 19890912 ; US 1992-933309 19920821; US 1994-231914 19940425; US 1995-467322 19950606**
IC ICM B01D037-00
ICS B01D021-26; B01D039-02
AB US 5543060 A UPAB: 19970516
A method for treating a blood prod. comprises: (a) centrifuging the blood prod. to form supernatant and sediment layers, where the sediment layer includes red blood cells; (b) sepg. the supernatant layer from the sediment layer by passing through a **filter** comprising a **porous** medium having a critical wetting surface tension (CWST) of 70-115 dynes/cm until the **filter** is blocked.
Pref. the blood prod. is whole blood obtd. from a human and mixed with anticoagulating agent and the supernatant layer is passed through the

porous medium within 8 hrs. of obtaining the blood from the human. The **porous** medium depletes the supernatant layer of >99.9% (esp. >99.99%) of leukocytes present. The blood prod. includes platelets. The medium has a negative zeta potential of -3 to -30 (esp. -7 to -20) millivolts at pH 7.3. The medium has CWST of 90-100 dynes/cm.

USE - Used for processing donated blood. The **porous** medium blocks red blood cells but allows the passage of platelets.

Dwg.1/2

FS CPI
FA AB; GI
MC CPI: A12-V03B; B04-B04D1; B11-B

L45 ANSWER 4 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1995-220779 [29] WPIX
DNC C1995-101719
TI Excluding DNA and RNA from prepn. - comprises filtering water soluble soln. through cellulose **porous** hollow yarn, then absorbing filtrate.
DC B04 D16
PA (ASAH) ASAHI KASEI KOGYO KK
CYC 1
PI JP 07133290 A 19950523 (199529)* 4p C07K001-34 <--
ADT JP 07133290 A **JP 1993-303299 19931110**
PRAI **JP 1993-303299 19931110**
IC ICM **C07K001-34**
ICS C12P021-00
AB JP 07133290 A UPAB: 19950727
Excluding nucleic acids, comprising: (1) filtering a water-soluble soln. contg. protein through a filter having a mean dia. of at most 75 nm; and (2) absorbing the filtrate.

The soln. is pref. pharmaceutical product produced by gene recombination, cell fusing, etc., for example, **blood** plasma fraction e.g. albumin, globulin, and anti-haemophilic **factor VIII** or IX **coagulant**, interferon and monoclonal antibody. The filter is pref. cellulose **porous** hollow yarn membrane regenerated by cupri-ammonium method.

USE/ADVANTAGE - Used for prodn., purificn., and sterilisation of pharmaceutical prods. Nucleic acid (DNA and RNA) in any condition can be efficiently excluded with a high protein recovery maintained, compared to the conventional methods such as absorption alone which cannot exclude DNA in composite and in particle conditions.

In an example, a culture soln. of hybridoma was filtered through a filter of 35 nm mean dia. formed of cellulose **porous** hollow yarn regenerated by cupri-ammonium method. The filtrate was then mixed with anion-exchange agarose particles equilibrated with phosphate buffer (pH 7.0), followed by stirring. After absorbing, the soln. was centrifuged for particle/DNA sepn. Protein recovery was found to be 90% after filtration and 80% after absorption. DNA exclusion was found to be 82% after filtration and 99.95% after absorption.

Dwg.0/0

FS CPI
FA AB; GI
MC CPI: B04-B04D4; B04-G01; B04-H05; **B04-H19**; B04-N02; B04-N04; D05-H12; D05-H13

L45 ANSWER 5 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1994-177817 [22] WPIX
DNC C1994-081287
TI Extracting **factor VIII - von Willebrand factor** complex from plasma - comprises stabilisation, selective absorption, extraction and purification, used for treatment of haemophilia A.
DC B04
IN ARRIGHI, S; BORRI, M G; BUCCI, E
PA (AIMA-N) AIMA-DERIVATI SPA; (ISTS) SCLAVO SPA; (ISIS-N) ISI IST SIEROVACCINOGENO ITAL SPA

CYC 11
PI EP 600480 A2 19940608 (199422)* EN 5p C07K013-00 <--
R: AT CH DE DK ES FR GB IT LI NL SE
EP 600480 A3 19941123 (199536) C07K013-00 <--
IT 1256622 B 19951212 (199627) A61K000-00 <--
EP 600480 B1 20000906 (200044) EN C07K014-755 <--
R: AT CH DE DK ES FR GB IT LI NL SE
DE 69329371 E 20001012 (200059) C07K014-755 <--
ADT EP 600480 A2 **EP 1993-119439 19931202**; EP 600480 A3 **EP 1993-119439 19931202**; IT 1256622 B **IT 1992-MI2778 19921204**; EP 600480 B1 **EP 1993-119439 19931202**; DE 69329371 E **DE 1993-629371 19931202, EP 1993-119439 19931202**
FDT DE 69329371 E Based on EP 600480
PRAI **IT 1992-MI2778 19921204**
REP No-SR.Pub; EP 303329; EP 416983; EP 468181; WO 8602838; WO 9005140
IC ICM A61K000-00; C07K013-00; **C07K014-755**
ICS C07K001-36; C07K003-20
AB EP 600480 A UPAB: 19940722
A process for extracting **Factor VIII - von willebrand factor** (FVIII:C-FvW) complex from total human plasma comprises: (a) stabilising unfrozen plasma (at room temp.) with antiprotease, or a basic amino acids or wino acids, contg. thiolic or indolic gps.; diluted in sterile and apyrogenic distilled water, in a vol. of Ca, 1/2 to 1/10th of the vol. of the plasma; (b) treating the mixt. with an anionic exchange resin conditioned to separate the **factors** constituting the protrombinic compled (PTC); (c) stabilising the PTC plasma supernatant with heparin and feeding into a chromatographic column contg. an anionic exchange resin suitably conditioned; (d) eluting the adsorbed **Factor VIII**:C - FvW complex upon the column and collecting the solution and stabilising it with heparin and polyethylene glycol (PEG) and treating it with an aluminium hydroxide, Al(OH)3, suspension; (e) **filtering** the supernatant contg. **Factor VIII**:C-FVW and restoring osmolarity conditions in the solution, then subjecting it to viral inactivation; (f) feeding the solution into a chromatographic column, contg. a conditioned cationic exchange resin; and (g) eluting the adsorbed **Factor VIII** :C-FVW complex and bringing the solution obtained to physiologic condition, conc. and dispensing into vials and lyophilisating.
USE - This method is useful for producing large quantities of **Factor VIII** concentrates for prophylaxis and treatment of haemophilia A.
Dwg.0/0
FS CPI
FA AB
MC CPI: **B04-H19**; B11-B; B14-F08

L45 ANSWER 6 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1991-369187 [50] WPIX
DNC C1991-159142
TI Isolation of high-purity **factor VIII** - by immuno-sorption after adding divalent ions.
DC A96 B04 D16
IN **CHTOUROU, A**
PA (NATR-N) FONDATION NAT TRANS
CYC 15
PI WO 9118017 A 19911128 (199150)* <--
RW: AT BE CH DE DK ES FR GB GR IT LU NL SE
W: CA US
FR 2662166 A 19911122 (199206) <--
ADT FR 2662166 A **FR 1990-6252 19900518**
PRAI **FR 1990-6252 19900518**
REP EP 123945; EP 152746; EP 286323
IC **A61K035-16; A61K037-47**; C07K003-18; C07K013-00
AB WO 9118017 A UPAB: 19930928
Isolation of high-purity **factor VIII** (FVIII) from aq. mixts. contg. FVIII complexed with **von Willebrand**

factor (**vWF**) is effected by (a) adding sufficient divalent ions to dissociate the FVIII-**vWF** complex, (b) contacting the mixt. with an immunosorbent comprising an anti-FVIII monoclonal antibody covalently immobilised on a rigid support, and (c) eluting FVIII from the immunosorbent. The antibody is directed against the light chain of FVIII, is capable of inhibiting the coagulant activity of FVIII:C, and is capable of binding to FVIII by strong hydrophobic interactions.

The starting material is plasma, solubilised cryoprecipitate, a prepurified FVIII concentrate, or a culture supernatant contg. recombinant FVIII. The divalent ions (esp. Ca2+) are added in a concn. of 0.1-0.6 (esp. 0.2-0.4)M. The antibody is 463A8 (Thrombosis and Haemostasis, 56/3), 271, 1986) and is immobilised on a high-porosity polyacrylamide gel in an amt. of 0.1-5 (esp. 0.3-1) mg/ml. The contact time in step (b) is less than 90 (esp. less than 60) min. when the FVIII/antibody ratio is 200-600 IU/mg. Elution is effected with a buffer soln. contg. a detergent. The eluate may be further purified by ion-exchange chromatography.

ADVANTAGE - Step (a) accelerates the immunosorption of FVIII in step (b) and increases the yield of purified FVIII (cf. EP286323).

0/4

FS CPI
FA AB
MC CPI: A12-V03C2; A12-W11L; B04-B04D3; D05-H13

L45 ANSWER 7 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1991-295372 [40] WPIX
DNC C1991-127660
TI Prepn. of **factor VIII** soln. of intermediate purity - starting from cryo-ppte. by solubilising, adding polysaccharide sulphate to ppte. fibrinogen and fibronectin, filtering, re-pptn. etc..
DC B04
IN **CHTOUROU, A**
PA (NATR-N) FOND NAT TRANSFUS S; (NATR-N) FONDATION NAT TRANS
CYC 15
PI WO 9113625 A 19910919 (199140)*
RW: AT BE CH DE DK ES FR GB GR IT LU NL SE
W: US
FR 2659557 A 19910920 (199148)
EP 472711 A 19920304 (199210)
R: AT BE CH DE ES FR GB IT LI LU NL SE
FR 2665364 A 19920207 (199215)
ADT FR 2659557 A FR 1990-3328 19900315; EP 472711 A EP 1991-906628 19910315; FR 2665364 A FR 1990-9828 19900801
PRAI FR 1990-3328 19900315; FR 1990-9828 19900801
REP EP 127603; EP 238701; EP 343275
IC **A61K035-16; A61K037-47**
AB WO 9113625 A UPAB: 19930928
A conc. soln. of **Factor VIII**, of intermediate purity, is prepd. from a cryo-pptd. by: (a) the cryoprecipitate is solubilised; (b) a polysaccharide sulphate (PSS) is added to the solution under conditions of temp. and concn. such that there is not pptn. of **Factor VIII** but fibrinogen and fibronectin are pptd.; (c) solid is removed from the supernatant liquid; (d) the liquid is submitted to a second pptn. by the addition of aluminium hydroxide gel. This pptes. vitamin K **factors** and other proteic contaminants, while leaving the **Factor VIII** in solution; (e) solid is removed from the supernatant liquid; and (f) liq. is the desired solution of **Factor VIII**.

USE/ADVANTAGE - **Factor VIII** is used in the treatment of haemophiliacs. The process is simple and gives a product that may either be used without further purifcn. or is suitable for further purifcn., e.g. by ion exchange chromatography or by gel filtration. @(16pp Dwg.No.0/2)

FS CPI
FA AB
MC CPI: B04-B04D3; B12-H04

L45 ANSWER 8 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1989-186244 [26] WPIX
DNC C1989-082330
TI Anti-haemophilic factor concentrate prodn. from cryo-precipitate - includes viral inactivation with chemical agent and gel **filtration** to remove agent and concentrate factor.
DC B04
IN BROCKWAY, W J; SENG, R L
PA (FARB) BAYER CORP; (MILE) MILES INC
CYC 14
PI EP 321835 A 19890628 (198926)* EN 11p <--
R: AT BE CH DE FR GB IT LI NL SE
AU 8827310 A 19890622 (198933) <--
JP 01301625 A 19891205 (199003) <--
US 5177191 A 19930105 (199304) 8p C07G007-00 <--
EP 321835 B1 19940928 (199437) EN 14p C07K003-12 <--
R: AT BE CH DE FR GB IT LI NL SE
US 5356878 A 19941018 (199441) 8p A61K035-14 <--
DE 3851696 G 19941103 (199443) C07K003-12 <--
CA 1339477 C 19970923 (199751) C07K001-36 <--
JP 2689390 B2 19971210 (199803) 10p C07K014-755 <--
ADT EP 321835 A **EP 1988-120808 19881213**; JP 01301625 A **JP 1988-316557 19881216**; US 5177191 A **Cont of US 1987-135966 19871221, US 1990-587815 19900924**; EP 321835 B1 **EP 1988-120808 19881213**; US 5356878 A **Cont of US 1987-135966 19871221, Div ex US 1990-587815 19900924, US 1993-852 19930104**; DE 3851696 G **DE 1988-3851696 19881213, EP 1988-120808 19881213**; CA 1339477 C **CA 1988-586473 19881220**; JP 2689390 B2 **JP 1988-316557 19881216**
FDT US 5356878 A Div ex US 5177591; DE 3851696 G Based on EP 321835; JP 2689390 B2 Previous Publ. JP 01301625
PRAI **US 1987-135966 19871221**
REP 4.Jnl.Ref; A3...9015; EP 104356; EP 123877; EP 131740; No-SR.Pub; WO 8403628; 2.Jnl.Ref
IC ICM A61K035-14; C07G007-00; C07K001-36; C07K003-12; **C07K014-755**
ICS A61K037-46; A61K038-17; **A61K038-37**; A61K038-43; A61K039-00; A61K039-12; C07K001-16; C07K001-30; C07K003-20; C07K013-00; C07K015-12
ICA A61K035-16
AB EP 321835 A UPAB: 19930923
Prodn. of antihaemophilic factor (AHF) concentrate from cryoppte. comprises (1) (a) dissolving the cryoppte.; (b) removing non-AHF proteins by pptn. with PEG; (c) treating AHF through a gel **filtration** column of size exclusion resin to remove the chemical and to concentrate the AHF to at least 35 units of FActor (VII) activity/ml pooled concentrate; or (2) (a) dissolving the cryoppte. to form AHF soln., (b) contacting the soln. with Al(OH)3 to form a suspension binding vitamin K-dependent protein; (c) pptg. the suspension with PEG at 20-25 deg.C to form an AHF-contg. effluent; and (d) pptg. AHF with a mixt. of glycine and NaCl.
USE/ADVANTAGE - Useful in treatment of haemophilia A. The process gives high yields of AHF with milder processing steps, the prod. being free of infectious agents, without loss of therapeutic or immunological activity.
0/0
FS CPI
FA AB
MC CPI: **B04-B04D3**; B12-H04
ABEQ US 5177191 A UPAB: 19930923
Process for prodn. of a concentrate of antihaemophilic **factor** (AHF) from cryoprecipitate comprises: (a) dissolving the cryoprecipitate; (b) removing non-AHF proteins by pptn. with PEG; (c) treating AHF with a chemical for viral inactivation; and (d) passing AHF through a gel **filtration** column contg. a size exclusion resin to remove the chemical and to isolate AHF to at least 35 U of **factor**

VIII activity/ml pooled concentrate.
USE/ADVANTAGE - AHF is highly pure. No loss of therapeutic or immunological activity. For treating haemophilia A.
0/0

ABEQ EP 321835 B UPAB: 19941109
A process for the production of a concentrate of anti-haemophilic **factor** (AHF) from cryoprecipitate comprising the steps of: (a) dissolving said cryoprecipitate; (b) removing non-AHF proteins by precipitation with polyethylene glycol (PEG); (c) treating said AHF with a chemical for viral inactivation; then (d) passing said AHF through a gel **filtration** column containing a size exclusion resin to remove said chemical and to isolate said AHF to at least 35 units of **Factor VIII** activity per ml of pooled concentrate.
Dwg.0/0

ABEQ US 5356878 A UPAB: 19941206
Antihaemophilic **factor** (AHF) concentrate free of non-human protein and viral agents has 1-10 mg HSA/ml reconstituted soln. and a **vWF**: AHF ratio of 0.75:2.00. The **factor** has a specific activity of at least 400/mg.
USE - Is of high specific activity and has desirable amts. of **vWF**.
Dwg.0/0

L45 ANSWER 9 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1987-356672 [51] WPIX
DNC C1987-152605
TI Automatic purificn. of physiologically active substances - by **filtration**, opt. **ultrafiltration** and affinity chromatography.
DC A96 B04 J01
IN HIROSHI, M; TOSHIHARU, M
PA (GREC) GREEN CROSS CORP
CYC 11
PI EP 249932 A 19871223 (198751)* EN 48p <--
R: BE CH DE ES FR GB LI NL SE
JP 62298536 A 19871225 (198806) <--
CA 1286696 C 19910723 (199134) <--
ADT EP 249932 A **EP 1987-108626 19870616**; JP 62298536 A **JP 1986-139142 19860617**
PRAI **JP 1986-139142 19860617**
REP 1.Jnl.Ref; A3...9016; EP 159025; EP 220966; No-SR.Pub; US 4568488
IC A61K037-02; A61K045-02; C07K003-28; C07K017-02; C12N009-00
AB EP 249932 A UPAB: 19930922
Process and appts. for automatic purificn. of a physiologically active substance are claimed.
The process comprises (a) **filtering** a soln. contg. (I) through at least one **filter** with a **pore** size of 0.22-500 microns; (b) opt. subjecting the **filtrate** to **ultrafiltration** to obtain a concentrate contg. (I) and a permeate contg. impurities with a lower molecular wt. than (I); and (c) subjecting the **filtrate** or concentrate to affinity chromatography to obtain a purified soln. of (I). Also claimed is a carrier with an antibody fixed thereto for recovering a protein from a cell culture soln., where the carrier is sterilised.
USE/ADVANTAGE - The process is esp. useful for recovering proteins from culture solns. of leucocytes, lymphoblasts, hybridomas, E. coli, B. subtilis or yeast, the protein being interferon, urokinase, pro-urokinase, kallikrein, lysozyme, trypsin inhibitor, human granulocyte-differentiation-inducing glycoprotein, interleukin, CSF, tissue plasminogen activator, B-cell growth factor, TNF, epidermal growth factor, lymphotoxin, a hormone, a monoclonal antibody, erythropoietin, antithrombin III, transferrin, plasminogen, plasminogen activator, alpha-fetoprotein or hepatitis B surface antigen. Automation reduces the time and labour required and facilitates maintenance of aseptic conditions.
0/3

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FS   CPI
FA   AB
MC   CPI: A12-V; A12-W11L; B02-V03; B04-B02C3; B04-B02D; B04-B04A6; B04-B04C1;
          B04-B04C5; B04-B04C6; B04-B04J; B04-C01G; B11-B; J01-C03; J01-D01A;
          J01-F02


=> d his

     (FILE 'HOME' ENTERED AT 11:07:16 ON 17 OCT 2001)
               SET COST OFF

     FILE 'WPIX' ENTERED AT 11:07:30 ON 17 OCT 2001
               E CHTOUROU A/AU
L1           3 S E3,E4
               E NOGRE M/AU
L2           1 S E3
               E PORTE P/AU
L3          11 S E3,E4
L4          13 S L1-L3
L5           3 S L4 AND A61K/IC,ICM,ICS
               E A61K-38-37/IC,ICM,ICS
               E A61K038-37/IC,ICM,ICS
L6          98 S E3-E5
               E A61K038-37/ICA,ICI
L7           2 S E4
               E A61K038:37/ICI
L8           2 S E3
L9        2010 S (B04-H19 OR C04-H19 OR B04-B04D3 OR C04-B04D3)/MC
L10       2338 S V613/M0,M1,M2,M3,M4,M5,M6
L11       3586 S L6-L10
L12        185 S BLOOD(L)COAGUL?(L)FACTOR(L)VIII
L13        514 S (BLOOD OR COAGUL?)(L)FACTOR(L)VIII
L14       1165 S FACTOR(L)VIII
L15        297 S VON(L)WILLEBRAN?(L)FACTOR
               E C07K014-755/IC,ICM,ICS
L16        149 S E3-E5
               E C07K014-755/ICA,ICI
L17          9 S E3
               E C07K014:755/ICI
L18       4274 S L11-L14,L16,L17
L19         18 S L18 AND C07K001-34/IC,ICM,ICS,ICA,ICI
L20        233 S L18 AND N104/M0,M1,M2,M3,M4,M5,M6
L21         90 S L18 AND (M423(S)M720(S)V613(S)N104)/M0,M1,M2,M3,M4,M5,M6
L22         17 S L21 AND (FILTER? OR FILTR?)
L23         19 S L21 AND (?FILTER? OR ?FILTR?)
L24         35 S L19,L22,L23
L25         37 S L5,L24
L26        112 S L18 AND (M423(S)M720(S)V613(S)N161(S)(N511 OR N512))/M0,M1,M2
L27         22 S L26 AND (?FILTER? OR ?FILTR?)
L28         55 S L25,L27
L29         53 S L28 AND (PY<=1997 OR PRY<=1997 OR AY<=1997)
L30          3 S L15 AND L29
L31          3 S VWF AND L29
L32          4 S L30,L31
L33          5 S L5,L32
L34         48 S L29 NOT L33
               SEL L34 DN 1 4 6 8 10-12 16 17 21 23-25 33-35 38 39 44 45 46
L35         27 S L34 NOT E1-E26
L36         16 S L35 AND FACTOR(S)(VIII OR 8)
L37          3 S L35 AND L6-L8
L38         16 S L36,L37
L39         19 S L5,L38

     FILE 'WPIX' ENTERED AT 12:28:32 ON 17 OCT 2001
L40         11 S L35 NOT L39
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L41          10 S (PORE OR POROS? OR POROUS?) AND L34
L42          11 S L33,L41 NOT L38
L43           6 S L42 AND FACTOR(L)(VIII OR 8)
L44          11 S L42,L43
L45           9 S L44 NOT (LEUKOPEN? OR BEAM )/TI

=> d his

     (FILE 'HOME' ENTERED AT 14:33:39 ON 17 OCT 2001)

     FILE 'REGISTRY' ENTERED AT 14:33:47 ON 17 OCT 2001
                SET COST OFF
                E BLOOD-COAGULATION FACTOR VIII/CN
L1            3 S E3
                E BLOOD COAGULATION FACTOR VIII NOT L1
L2          698 S BLOOD COAGULATION FACTOR VIII NOT L1
L3            1 S CALCIUM/CN
                E CALCIUM, ION/CN
L4            1 S E23
                E CALCIUM CHLORIDE/CN
L5            1 S E28
L6            2 S 9005-49-6 OR 9041-08-1

     FILE 'HCAPLUS' ENTERED AT 14:35:22 ON 17 OCT 2001
L7          620 S (L1 OR L2)(L)(PREP OR PUR)/RL
L8         4937 S (BLOOD OR COAGULAT? OR CLOT?)(L)FACTOR(L)VIII
L9         7455 S FACTOR(L)VIII
L10        7455 S L8,L9
L11        6903 S L1 OR L2
L12        9865 S L10,L11
L13         620 S L7 AND L12
L14           5 S L12 AND (CHTOUROU A? OR NOGRE M? OR PORTE P?)/AU
L15           3 S L14 NOT (GLUE OR APROTININ)/TI
L16         602 S L12 AND (L3 OR L4 OR L5 OR CACL2 OR CA2 OR (CA OR CALCIUM)()C
L17         535 S L12 AND (L6 OR HEPARIN)
L18         110 S L13 AND L16,L17
L19           1 S L12 AND PLANOV?
L20           3 S L15,L19
L21           3 S L20 AND L16-L18
L22        7857 S L12 AND (PY<=1997 OR PRY<=1997 OR AY<=1997)
L23         906 S L22 AND L16,L17
L24         101 S L23 AND L13
                E FILTRATION/CT
                E E3+ALL
L25       15312 S E3,E2+NT
                E FILTER/CT
                E E19+ALL
L26        4392 S E1
                E E2+ALL
L27       34487 S E5,E6,E3+NT
L28        6715 S E33,E34,E35
L29          30 S L22 AND L25-L28
L30         606 S L22 AND (?FILTER? OR ?FILTR?)
L31          28 S L29,L30 AND (PORE OR POROS? OR POROUS?)
L32          35 S L29,L30 AND (?PORE? OR ?POROS? OR ?POROUS?)
L33          35 S L31,L32
L34           7 S L33 AND L23
L35           5 S L33 AND L24
L36           7 S L34,L35
L37          19 S L13 AND L25-L28
L38         102 S L13 AND (?FILTR? OR ?FILTER?)
L39           7 S L37,L38 AND (CATION? OR DISSOCIAT?)
L40           5 S L22 AND L39
L41          13 S L15,L36,L40 AND L22
L42         121 S L22 AND (?PORE? OR ?POROS? OR ?POROUS?)
L43          35 S L42 AND (?FILTER? OR ?FILTR?)
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L44            8 S L42 AND L25-L28
L45           35 S L43,L44
L46           28 S L45 NOT L41
L47           22 S L11 AND L46
L48         4484 S VON(L)WILLEBRAN?(L)FACTOR
L49            3 S L46 AND L48
L50            1 S L46 AND  VWF
L51           22 S L47,L49,L50
L52            6 S L46 NOT L51
                 SEL HIT RN L51

     FILE 'REGISTRY' ENTERED AT 14:50:11 ON 17 OCT 2001
L53            2 S E1-E2

     FILE 'HCAPLUS' ENTERED AT 14:50:19 ON 17 OCT 2001
L54           22 S L51 AND L7-L52
L55            7 S L45 NOT L46
L56           29 S L54,L55
L57           29 S L56 AND L7-L55
L58           29 S L56 AND L12,L3-L6
L59            8 S L56 AND (CA OR CA2 OR CALCIUM OR CACL2 OR CALCIUM CHLORIDE OR
L60            1 S L56 AND CHAOTROP?
L61           29 S L56-L60
                 SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 14:53:03 ON 17 OCT 2001
L62            6 S E3-E8

=> fil reg

FILE 'REGISTRY' ENTERED AT 14:53:25 ON 17 OCT 2001
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STRUCTURE FILE UPDATES:   16 OCT 2001  HIGHEST RN 362587-51-7
DICTIONARY FILE UPDATES:  16 OCT 2001  HIGHEST RN 362587-51-7

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER see
HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d ide can tot


L62  ANSWER 1 OF 6  REGISTRY  COPYRIGHT 2001 ACS
RN   113189-02-9  REGISTRY
CN   Blood-coagulation factor VIII, procoagulant (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   AHF-A
CN   Antihemophilic factor
CN   Antihemophilic factor A
CN   Antihemophilic globulin
CN   Bioclate
CN   Blood-coagulation factor VIII
CN   Blood-coagulation factor VIIIc
CN   Coagulation factor VIIIc
```

CN Factor VIII
CN Monoclate
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, CA, CAPLUS, CBNB, CEN, CIN, DIOGENES, DRUGNL, DRUGPAT, DRUGUPDATES, IPA, MSDS-OHS, PHAR, PIRA, PROMT, TOXLINE, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1271 REFERENCES IN FILE CA (1967 TO DATE)
36 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1278 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:239982

REFERENCE 2: 135:239980

REFERENCE 3: 135:238455

REFERENCE 4: 135:226369

REFERENCE 5: 135:225959

REFERENCE 6: 135:222352

REFERENCE 7: 135:209300

REFERENCE 8: 135:208642

REFERENCE 9: 135:207196

REFERENCE 10: 135:206422

L62 ANSWER 2 OF 6 REGISTRY COPYRIGHT 2001 ACS
RN **109319-16-6** REGISTRY
CN Blood-coagulation factor VIII, von Willebrand's (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Antigens, blood-coagulation factor VIII-related
CN Blood platelet-aggregating factor
CN Blood-coagulation factor VIII
CN Blood-coagulation factor VIII antigen
CN Blood-coagulation factor VIII-related antigen
CN Blood-coagulation factor VIIIR
CN Factor VIII
CN Ristocetin cofactor
CN Ristocetin-von Willebrand factor
CN von Willebrand's factor
MF Unspecified
CI MAN
SR CA
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CEN, CIN, EMBASE, IPA, PIRA, PROMT, TOXLINE, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
2790 REFERENCES IN FILE CA (1967 TO DATE)
65 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2797 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:240437

REFERENCE 2: 135:240313

REFERENCE 3: 135:240163

REFERENCE 4: 135:240162

REFERENCE 5: 135:240137

REFERENCE 6: 135:239980

REFERENCE 7: 135:238945

REFERENCE 8: 135:238357

REFERENCE 9: 135:236941

REFERENCE 10: 135:236216

L62 ANSWER 3 OF 6 REGISTRY COPYRIGHT 2001 ACS
RN **10043-52-4** REGISTRY
CN Calcium chloride (CaCl2) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Calcium chloride (8CI)
OTHER NAMES:
CN Bovikalc
CN Calcium dichloride
CN Calcium(2+) chloride
CN Calcosan
CN Calol
CN Calzina oral
CN Daraccel
CN Dowflake
CN Liquidow
CN Peladow
CN Stopit
CN U-Ramin MC
DR 139468-93-2
MF Ca Cl2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, TULSA, USAN, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

Cl—Ca—Cl

27376 REFERENCES IN FILE CA (1967 TO DATE)
205 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
27414 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:249513

REFERENCE 2: 135:249413

REFERENCE 3: 135:247187

REFERENCE 4: 135:247104

REFERENCE 5: 135:246742

REFERENCE 6: 135:246472

REFERENCE 7: 135:246168

REFERENCE 8: 135:245263

REFERENCE 9: 135:244328

REFERENCE 10: 135:243969

L62 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2001 ACS
RN **9005-49-6** REGISTRY
CN Heparin (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN .alpha.-Heparin
CN Bemiparin
CN Certoparin
CN Clexane
CN Clivarin
CN Clivarine
CN CY 216
CN CY 222
CN Dalteparin
CN Enoxaparin
CN Fluxum
CN FR 860
CN Fragmin A
CN Fragmin B
CN Fraxiparin
CN Heparin sulfate
CN Heparinic acid
CN KB 101
CN Multiparin
CN Novoheparin
CN OP 386
CN OP 622
CN Pabyrn
CN Parnaparin
CN Parvoparin
CN Reviparin
CN Sandoparin
CN Sublingula
CN Vetren
CN Vitrum AB
DR 9075-96-1, 11078-24-3, 11129-39-8, 104521-37-1, 37324-73-5, 91449-79-5
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyester, Polyester formed
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
17456 REFERENCES IN FILE CA (1967 TO DATE)
1746 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
17496 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:242436

REFERENCE 2: 135:240606

REFERENCE 3: 135:240537

REFERENCE 4: 135:238962

REFERENCE 5: 135:238948

REFERENCE 6: 135:238331

REFERENCE 7: 135:238233

REFERENCE 8: 135:236729

REFERENCE 9: 135:236433

REFERENCE 10: 135:236410

L62 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2001 ACS
RN **9001-27-8** REGISTRY
CN Blood-coagulation factor VIII, complex (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Blood-coagulation factor VIII
CN Factor VIII
CN Factorate
CN Hemofil
CN Hemofil M
CN Profilate
CN Thromboplastinogen
DR 9035-62-5, 114046-09-2
MF Unspecified
CI COM, MAN
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CEN, CHEMLIST, CIN, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
3161 REFERENCES IN FILE CA (1967 TO DATE)
63 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3166 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:238614

REFERENCE 2: 135:225564

REFERENCE 3: 135:215820

REFERENCE 4: 135:209603

REFERENCE 5: 135:179815

REFERENCE 6: 135:151489

REFERENCE 7: 135:150968

REFERENCE 8: 135:150530

REFERENCE 9: 135:132089

REFERENCE 10: 135:127158

L62 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2001 ACS
RN **7440-70-2** REGISTRY
CN Calcium (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:

CN Atomic calcium
CN Blood-coagulation factor IV
CN Calcium atom
CN Calcium element
CN Praval
DR 8047-59-4
MF Ca
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHARMASEARCH, PIRA, PROMT, TOXLINE, TOXLIT, TULSA, ULIDAT, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

Ca

270961 REFERENCES IN FILE CA (1967 TO DATE)
6037 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
271261 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 135:251059

REFERENCE 2: 135:251043

REFERENCE 3: 135:251025

REFERENCE 4: 135:250983

REFERENCE 5: 135:250969

REFERENCE 6: 135:250929

REFERENCE 7: 135:250903

REFERENCE 8: 135:250730

REFERENCE 9: 135:250483

REFERENCE 10: 135:250340

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=> d bib abs hitrn tot l61

L61 ANSWER 1 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:404998 HCAPLUS
DN 131:49441
TI Method for preparing virus-free **factor VIII** solution by **filtration**
IN **Chtourou, Abdessatar; Nogre, Michel; Porte, Pierre**
PA Laboratoire Francais du Fractionnement et des Biotechnologies, Fr.
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9931138	A1	19990624	WO 1998-FR2715	19981214 <--
	W: AU, CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	FR 2772381	A1	19990618	FR 1997-15888	19971215 <--
	FR 2772381	B1	20010608		
	AU 9915681	A1	19990705	AU 1999-15681	19981214 <--
	EP 1037923	A1	20000927	EP 1998-959975	19981214 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	FR 1997-15888	A	19971215 <--		
	WO 1998-FR2715	W	19981214		

AB The invention concerns a method for prepg. by **filtration** a **factor VIII** soln. which is essentially free of virus and high mol. wt. vWF. The method comprises prepg. a soln. contg. high or very high purity **factor VIII** essentially free of high mol. wt. **VIII**-vWf complexes and **filtering** the soln. with a hydrophilic **filter** with **porosity** as low as 15 nm, such as **Planova** 15N (Asahi Chem.). **Chaotropic** ions, such as provided by **CaCl2**, may be used to effectuate the **dissocn.** The type of divalent ion and its concn. affected the yield. 0.35M **CaCl2** is preferred. Both **filtration** pressure and temp. were found to affect the yield: pressure less than that recommended by the manufacturer is used and the temp. is advantageously about 35.degree..

IT **7440-70-2, Calcium**, uses **10043-52-4, Calcium chloride**, uses
RL: MOA (Modifier or additive use); USES (Uses)
(method for prepg. virus-free **factor VIII** soln. by **filtration**)

IT **113189-02-9P, Blood-coagulation factor VIII**
RL: **PUR (Purification or recovery); PREP (Preparation)**
(method for prepg. virus-free **factor VIII** soln. by **filtration**)

IT **109319-16-6**
RL: REM (Removal or disposal); PROC (Process)
(method for prepg. virus-free **factor VIII** soln. by

filtration)
RE.CNT 5
RE
(1) Armour Pharma; EP 0197554 A 1986 HCAPLUS
(2) Association D'Aquitaine Pour Le Developpement De La Transfusion Sangui; EP 0383645 A 1990 HCAPLUS
(3) Fond Nat Transfusion Sanguine; WO 9118017 A 1991 HCAPLUS
(4) Pharmacia AB; WO 9600237 A 1996 HCAPLUS
(5) Sclavo Spa; EP 0468181 A 1992 HCAPLUS

L61 ANSWER 2 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:282075 HCAPLUS
DN 130:316644
TI Encapsulation method using biodegradable polymers
IN Laakso, Timo; Reslow, Mats
PA Bioglan Therapeutics AB, Swed.
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9920253	A1	19990429	WO 1998-SE1717	19980924	<--
	W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	SE 9703874	A	19990424	SE 1997-3874	19971023	<--
	SE 512663	C2	20000417			
	AU 9894670	A1	19990510	AU 1998-94670	19980924	<--
	AU 732891	B2	20010503			
	EP 1033973	A1	20000913	EP 1998-948005	19980924	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
	ZA 9809199	A	19990415	ZA 1998-9199	19981008	<--
	NO 2000002039	A	20000613	NO 2000-2039	20000418	<--
PRAI	SE 1997-3874	A	19971023	<--		
	WO 1998-SE1717	W	19980924			

AB This invention provides a novel method of encapsulating an active substance in a biodegradable polymer, which comprises: (a) dissolving the biodegradable polymer in an org. solvent; (b) dispersing the active substance in the org. soln. obtained in step (a) to provide a dispersion with the active substance as the inner phase thereof, or alternatively, emulsifying the active substance, dissolved in water or other aq. solvent, in the org. soln. obtained in step (a) to provide an emulsion with the active substance as the inner aq. phase; and (c) subjecting the dispersion or emulsion to an encapsulation operation with an aq. polyethylene glycol soln. as a continuous phase to provide micro- or nanoparticles having the active substance encapsulated therein. A soln. of glycolide-lactide copolymer was prepd. by dissolving the polymer in EtOAc, then bovine serum albumin dissolved in a phosphate buffer was added to the polymer soln. The obtained homogeneous dispersion was slowly injected into the soln. of polyethylene glycol with stirring. Deionized water was added to reduce the viscosity of the suspension for **filtration** using a **Millipore** membrane. The **filtrate** was washed with water and dried to obtain spherical microparticles.
IT **9001-27-8**, **Factor VIII**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microencapsulation of biol. active agents in biodegradable polymers in the absence of surfactants)
RE.CNT 5

RE
(1) Fong, J; US 4384975 A 1983 HCAPLUS
(2) Nuwayser, E; US 4568559 A 1986 HCAPLUS
(3) Okada, C; US 4652441 A 1987 HCAPLUS
(4) Syntex Inc; EP 0052510 A2 1982 HCAPLUS
(5) Tice, T; US 5407609 A 1995

L61 ANSWER 3 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:604921 HCAPLUS
DN 129:207257
TI Method for removing viruses from protein solution by **nanofiltration**
IN Hiemstra, Harry; Ter Hart, Hendricus Gerardus Josephus; Prins-de Nijs, Ingrid Margaretha Maria; Hoek, Pieter Johannes; Over, Jan
PA Stichting Sanquin Bloedvoorziening, Neth.
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9837086	A1	19980827	WO 1998-NL108	19980223
	W: CA, CN, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 979237	A1	20000216	EP 1998-908308	19980223 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, IE, FI				
PRAI	EP 1997-200533		19970224 <--		
	WO 1998-NL108		19980223		

AB Disclosed is a method for removing viruses, in particular small non-envelopped viruses, from a plasma-derived product, such as Prothrombin Complex Conc. The method comprises **prefiltration** to remove contaminating high mol. wt. proteins, followed by **nanofiltration** through a membrane with an av. **pore** size of 15 nm. The method is capable or removing >5.1 log Canine parvovirus and >6.0 log Hepatitis A virus.
IT **9001-27-8 109319-16-6**
RL: REM (Removal or disposal); PROC (Process)
(method for removing large proteins and virus from blood products by **prefiltration** and **nanofiltration**)

L61 ANSWER 4 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:585862 HCAPLUS
DN 129:193701
TI Method for removing viruses from a protein solution
PA Stichting Centraal Laboratorium van de Bloedtransfusiedienst van het Nederla, Neth.
SO Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 860444	A1	19980826	EP 1997-200533	19970224 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
	EP 979237	A1	20000216	EP 1998-908308	19980223 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, IE, FI				
PRAI	EP 1997-200533		19970224 <--		
	WO 1998-NL108		19980223		

AB A method for removing viruses, in particular small non-enveloped viruses, from a plasma derived product, such as Prothrombin Complex Conc. comprises **prefiltration** to remove contaminating high mol. wt. proteins, followed by **nanofiltration** through a membrane with an av. **pore** size of 15 nm. The method is capable of removing > 5.1 log

Canine parvovirus and > 6.0 log Hepatitis A virus.

IT **9001-27-8P, Factor VIII 109319-16-6P**
, Factor VIII
RL: PEP (Physical, engineering or chemical process); **PUR**
(Purification or recovery); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; PROC (Process); USES (Uses)
(virus removal from protein solns.)

L61 ANSWER 5 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:861727 HCAPLUS
DN 123:309817
TI Permeation mechanism of DNA molecules in solution through cuprammonium regenerated cellulose hollow fiber (BMM)
AU Hirasaki, Tomoko; Sato, Tetsuo; Tsuboi, Takashi; Nakano, Hiroo; Noda, Toshiaki; Kono, Akira; Yamaguchi, Kazuhito; Imada, Kiyohisa; Yamamoto, Naoki; et al.
CS BMM Development and Business Promotion Department, Asahi Chemical Ind. Co., Ltd., The Imperial Tower 18F, 1-1-1 Uchisaiwaicho, Chiyoda-ku, Tokyo, 100, Japan
SO J. Membr. Sci. (**1995**), 106(1-2), 123-9
CODEN: JMESDO; ISSN: 0376-7388
DT Journal
LA English
AB The authors tried to clarify the membrane permeation mechanism of biopolymer DNA mol. in soln. through cuprammonium regenerated cellulose hollow fiber (BMM) from the dependence of the permeability of the DNA mol. on the mol. wt. (MW), transmembrane pressure (.DELTA.P), total challenge dose, original concn. of DNA and conformation of DNA, and from observation of the shape of the DNA mol. remaining in the membrane wall. The shape of the DNA mol. was obsd. using TEM. The permeability of DNA mols. decreased with an increase in the MW of the DNA mol. The MW of the mol. which showed a permeability of >0.9 was 1 .times. 106 for the protein with global configuration and 1 .times. 108 for DNA. The linear protein **blood-coagulation factor VIII** combined with **von Willebrand factor** (F-**VIII** with **vWF**) with MW of 2 .times. 107 showed permeability similar to that of DNA rather than that of the global protein. When .DELTA.P decreased, the permeability of DNA decreased. Electron microscope observation showed that the DNA mols. were elongated by the shear stress originated in the flow of the soln. in **pores**. Apparently, protein and DNA permeate through BMM mainly based on sieving effects. Mols. of DNA and F-**VIII** with **vWF** are considered to deform into a string shape along the stream line. The chem. structure of a mol. and the shear stress of **filtration** govern its deformability; the deformation of the mol. contributes to the permeability through BMM. The sieving effect in working on the permeation of mols. should take into account their deformability in addn. to their geometric size.

IT **9001-27-8, Blood-coagulation factor VIII**
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(permeation mechanism of DNA in soln. through cuprammonium regenerated cellulose hollow fiber)

L61 ANSWER 6 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:826252 HCAPLUS
DN 123:237742
TI Protein-platelet and platelet-leukocyte interaction at materials in contact with human blood
AU Nygren, H.ovrhdot.akan; Braide, Magnus; Karlsson, Christin
CS Dep. Anatomy Cell Biol., Univ. Goeteborg, Goeteborg, Swed.
SO J. Vac. Sci. Technol., A (**1995**), 13(5), 2613-18
CODEN: JVTAD6; ISSN: 0734-2101
DT Journal
LA English
AB The adhesion and activation of platelets and leukocytes at blood-material

interfaces was studied by fluorescence microscopy and photometry using specific anti-CD antibodies, antiplasma protein antibodies, and the **calcium** probe Fura-2. Hydrophilic glass or siliconized hydrophobic glass was prepd. and capillary blood was placed as droplets on the surface in a humified chamber. The adsorption of plasma proteins was monitored with FITC-labeled antibodies directed against albumin, IgG, fibrinogen, fibronectin, the **von Willebrand factor**, prothrombin/thrombin, and complement **factor** C3c. The adhesion of platelets was shown by anti-CD 61 antibodies, specific for this cell type. Adhesion of leukocytes was measured by staining their DNA with acridine orange. Adhering platelets were found after 15 s of blood-material contact on both surfaces. The no. of adhering platelets rapidly decreased at the hydrophilic surface, but remained high for more than 8 min at the hydrophobic surface. Fibrinogen was the dominating protein at the material surface, whereas fibronectin and the v. **Willebrand factor** were found at the cell surfaces. Platelet-derived microvesicles were found after 4 and 8 min of blood-material contact. These microvesicles showed intense staining with anti-C3 antibodies. Significant nos. of leukocytes (PMN cells) were seen after 2 h of blood-material contact. In other expts., granulocytes were isolated and incubated with Fura-2. The supernatant of hirudin-treated blood, exposed to hydrophilic or hydrophobic glass surfaces, was added to the cells and the fluorescence was recorded after emission at 340 and 380 nm. A rapid peak was seen, indicating **calcium** influx into the cytoplasm. The activating substance was removed from the supernatant by **filtering** it through a 0.1-0.45 .mu.m **Millipore filter**. The blood samples were taken from patients undergoing treatment with **extracorporeal** circulation. The samples were incubated with monoclonal antibodies against surface antigens CD-11b, 16, 35, 61 and 62. The fluorescence was measured in a flow cytofluorometer. The PMN cells were activated rapidly after the onset of oxygenator circulation.

IT **109319-16-6**
RL: BPR (Biological process); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(adhesion and activation of platelets and leukocytes at blood-material interfaces)

L61 ANSWER 7 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1993:576950 HCAPLUS
DN 119:176950
TI Spectrophotometric evaluation of the adhesion of blood platelets to collagen and microfibrils
AU Fauvel-Lafeve, F.; Meric, A.; Arbeille, B.; Tabaka, V.; Legrand, Y. J.
CS Hop. St.-Louis, Paris, 75010, Fr.
SO Thromb. Res. (**1993**), 71(3), 193-204
CODEN: THBRAA; ISSN: 0049-3848
DT Journal
LA English
AB The authors present an easy method in which the adhesion of platelets to collagen or to microfibrils was measured in a spectrophotometer, after an incubation of hypercitrated platelet rich plasma (PRP), or of a platelet suspension, with an inducer, followed by the **filtration** of non-adhering platelets through translucent **Isopore** membrane **filters** (**pore** diam. = 5 .mu.m). The adhering platelets, which are retained on the **filter**, were stained by Coomassie blue to quantify the adhesion by the simple reading of the O.D. 580 nm of the stained platelets which appear as a blue spot on the translucent membranes.

IT **109319-16-6**
RL: ANST (Analytical study)
(blood platelets adhesion to collagen and microfibrils response to)

L61 ANSWER 8 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1993:567716 HCAPLUS
DN 119:167716

TI Removal of thrombosis-inducing **Von Willebrand factors** from blood by **filtration**
IN Itagaki, Ichiro; Shimizu, Yoshihiro; Fukuyama, Mayumi
PA Toray Industries, Japan
SO Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 05168705	A2	19930702	JP 1992-147346	19920608 <--
PRAI	JP 1991-138746		19910611 <--		

AB A convenient method for removing the thrombosis-inducing high-mol. fraction of the **Von Willebrand factor** from blood by membrane **filtration** is described. A **filtration** app. contg. a **porous** membrane of 0.15.apprx.0.4 .mu.M **pore** size is employed. The method was demonstrated using a polysulfone membrane and a variety of other membranes.
IT **109319-16-6**
RL: BIOL (Biological study)
(removal from blood of, by membrane **filtration**)

L61 ANSWER 9 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1993:109835 HCAPLUS
DN 118:109835
TI **Porous** materials for separation of blood-coagulation factors
IN Yamaguchi, Masato; Morita, Hiroshi; Yamamoto, Tetsuo; Motozato, Yoshiaki
PA Kurita Water Industries, Ltd., Japan; Yamamoto, Tetsuro; Motosato, Yoshiaki
SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 04300835	A2	19921023	JP 1991-67059	19910329 <--

AB **Porous** materials having di(lower)alkylamino(lower)alkyl group(s) and mol. wt. exclusion limit of .gtoreq.5.0 .times. 105 are used for sepn. of **blood coagulation factors**, useful for treatment of hemophilia, etc. Purified konjak glucomannan was swelled in formamide, mixed with pyridine, and treated with Ac2O at 55.degree. for 4 days to give an acetate. The acetate was dissolved in CHCl3 with decalin, the soln. was added dropwise to an aq. soln. contg. 1 wt.% of 90% sapond. poly(vinyl alc.) at 55.degree., stirred for 24 h, cooled, **filtered**, and the spherical particles were washed, sapond. in 10 N aq. NaOH-MeOH for 2 h, **filtered**, and the particles were crosslinked in acetone-DMF-epichlorohydrin, and the particles were collected and washed with H2O and acetone to give crosslinked glucomannan particles. The glucomannan gel was treated with an aq. 5 N NaOH at 0.degree. for 1 h, treated with 2-(diethylamino)ethyl chloride HCl salt at 80.degree. for 1 h, **filtered**, the gel particles were washed with H2O, treated with an aq. 0.2 N NaOH, and washed with H2O to give DEAE-glucomannan gel. The gel adsorbed 92-95% of human **blood-coagulation factor VIII.**
IT **9001-27-8P, Blood-coagulation factor VIII**
RL: **PUR (Purification or recovery); PREP (Preparation)**
(purifn. of, for hemophilia treatment, crosslinked glucomannan-DEAE **porous** gel in)

L61 ANSWER 10 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1992:79885 HCAPLUS
DN 116:79885
TI An immunoassay or binding assay using internal calibration to measure the

amount of analyte in a sample
IN Selmer, Johan; Poulsen, Fritz
PA Novo-Nordisk A/S, Den.
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9119196	A1	19911212	WO 1991-DK151	19910606 <--
	W: AU, BG, CA, FI, HU, JP, KR, NO, PL, RO, SU, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	ZA 9104068	A	19920325	ZA 1991-4068	19910529 <--
	AU 9179678	A1	19911231	AU 1991-79678	19910606 <--
	EP 532627	A1	19930324	EP 1991-911152	19910606 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 05508013	T2	19931111	JP 1991-510326	19910606 <--
	US 5387503	A	19950207	US 1992-938039	19921112 <--
PRAI	DK 1990-1380		19900606 <--		
	WO 1991-DK151		19910606 <--		

AB A method of detg. the amt. of test analyte in a sample using internal calibration comprises: (a) mixing a sample with a predetd. amt. of a calibrator analyte foreign to the sample and with a comparable behavior in an assay to that of the test analyte; (b) contacting the mixt. (a) with a solid support contg., each in a sep. area, a reagent for binding the test and calibrator analytes, resp.; (c) contacting the solid support with a mixt. of labeled reagents for binding the test and calibrator analytes, resp.; and (d) detg. the amt. of test analyte in the sample by comparing the levels of labeled reagent bound to the test and calibrator analytes. Thus, EIA of creatine kinase M and B subunit (CK-MB) in serum samples uses myoglobin as internal calibrator. Test CK-MB-contg. serum samples with addn. of human myoglobin were added to each well of a Biodot **Microfiltration** App. (membrane) consisting of a well sensitized with monoclonal antibody to human CK B subunit, a 2nd well sensitized with monoclonal antibody to human myoglobin, and a control well without sensitization. This was followed by adding a mixt. of horseradish peroxidase-labeled anti-human CK M subunit monoclonal antibody and horseradish peroxidase-labeled anti-human myoglobin monoclonal antibody. One min. after the addn., the membrane was washed and treated with a substrate soln. The response was read by a reflectometer and the measured reflectance was transformed according to the Kubelka-Munk equation for CK-MB detn. The myoglobin-calibrated CK-MB assay was able to quantitate the CK-MB concn. in serum and the values compared well to those obtained by conventional calibration using a set of CK-MB calibrators. A kit for the anal. also is claimed.

IT **9001-27-8, Factor VIII**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, in body fluids, by immunoassay or binding assay, internal calibration in)

L61 ANSWER 11 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1991:602736 HCAPLUS
DN 115:202736
TI Membrane affinity purification apparatus and its use in the purification of macromolecules of therapeutic value
IN Goffe, Randal A.; Zale, Stephen E.; O'Connor, James L.; Kessler, Stephen B.; Cohen, Charles M.
PA Sepracor, Inc., USA
SO PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 9005018 A1 19900517 WO 1989-US4847 19891030 <--
W: AU, BB, BG, BR, DK, FI, HU, JP, KR, LK, MC, MG, MW, NO, RO, SD, SU
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, FR, GA, GB, IT, LU, ML, MR, NL, SE, SN, TD, TG
CA 2001720 AA 19900430 CA 1989-2001720 19891027 <--
AU 8945247 A1 19900528 AU 1989-45247 19891030 <--
EP 483143 A1 19920506 EP 1989-912702 19891030 <--
EP 483143 B1 19940601
EP 483143 B2 19970409
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE
AT 106272 E 19940615 AT 1989-912702 19891030 <--
US 5310688 A 19940510 US 1993-35549 19930323 <--
US 5683916 A 19971104 US 1995-465479 19950605 <--
PRAI US 1988-265061 19881031 <--
US 1989-428263 19891026 <--
US 1989-428263 19891026 <--
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EP 1989-912702 19891030 <--
WO 1989-US4847 19891030 <--
US 1990-487668 19900302 <--
US 1993-83859 19930628 <--

AB An app. is provided which is useful for the sepn. of .gtoreq.1 preselected ligate(s) in a fluid. Also provided is an easily scaled-up membrane affinity sepn. process which is reliable, highly selective, gives a high yield of product, and has a high volumetric throughput. A substantially isotropic **porous** membrane is used, to which is assocd. a preselected ligand, which provides an optimum loading capacity and low dead vol. while allowing high **filtrate** flow rates. Methods for isolation of macromols. of therapeutic value, e.g. **factor VIII** and fibronectin, are described, and diagrams of the app. are included. Cloning and expression of a bifunctional binding site protein (one domain binding digoxin and the other binding Ig Fc regions) are also described. Thus a polyether sulfone/poly(ethylene oxide) hollow-fiber membrane was sequentially reacted with ethylene glycol diglycidyl ether and hydroxyethyl cellulose, activated with 2-fluoro-1-methylpyridinium p-toluenesulfonate, and the activated fibers reacted with an antibody to **factor VIII**. The resulting membrane was used to purify a **factor VIII** conc.; the purifn. **factor** was 115.

IT **9005-49-6D, Heparin**, polymer-linked conjugates
RL: ANST (Analytical study)
(in affinity hollow-fiber membrane, for biomol. sepn.)

IT **9001-27-8, Blood-coagulation factor VIII**
RL: PROC (Process)
(sepn. of, with affinity hollow-fiber membrane)

L61 ANSWER 12 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1991:566440 HCAPLUS
DN 115:166440
TI Evaluation of wet pasteurization of a **factor VIII** concentrate produced by controlled-**pore** silica adsorption
AU Hiemstra, H.; Nieuweboer, Carina E. F.; Idoe, M. A.; Claassen, Jolien E.; Vos, Aster H. V.; Tersmette, M.; Strengers, P. F. W.; Over, J.; Mauser-Bunschoten, Eveline P.; et al.
CS Cent. Lab., Neth. Red Cross Blood Transfus. Serv., Amsterdam, NL-1006 AD, Neth.
SO Folia Haematol. (Leipzig) (**1990**), 117(4), 557-63
CODEN: FOHEAW; ISSN: 0323-4347
DT Journal
LA English
AB In the routine prodn. of a **factor VIII** (I) conc. (produced by the adsorption of contaminating proteins in cryoppts. on to controlled-**pore** SiO2 and concn. of the effluent by

ultrafiltration), the terminal dry-heat treatment (72 h at 60.degree.) was replaced by pasteurization (10-11 h at 60.degree.) in the liq. state. High effectivity of this procedure with respect to virus inactivation was demonstrated with a variety of both lipid-protein-enveloped model viruses, including HIV. Pair-wise quality control of dry-heated and pasteurized product revealed no differences, except in the compn. of the formulation buffer. A clin. study with hemophilia A patients showed the pasteurized product was well tolerated and the in vivo recovery and half-life of I were in the same (normal) range as found for the dry-heated counterpart.

IT **9001-27-8, Blood coagulation factor VIII**
RL: BIOL (Biological study)
(conc., hepatitis non-A non-B deactivation in, pasteurization vs.; dry heating for, model study of)

L61 ANSWER 13 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1991:415572 HCAPLUS
DN 115:15572
TI Virus inactivation in blood products by sodium thiocyanate and **ultrafiltration**
IN Hrinda, Michael E.; D'Alisa, Rose; Tarr, George Crissman
PA Rorer International (Overseas), Inc., USA
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9015613	A1	19901227	WO 1990-US3355	19900613	<--
	W: CA, JP					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE					
	CA 2034489	AA	19901216	CA 1990-2034489	19900613	<--
	CA 2034489	C	19960716			
	EP 431129	A1	19910612	EP 1990-909877	19900613	<--
	EP 431129	B1	19960529			
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE					
	JP 04501429	T2	19920312	JP 1990-509881	19900613	<--
	AT 138575	E	19960615	AT 1990-909877	19900613	<--
	ES 2087156	T3	19960716	ES 1990-909877	19900613	<--
	US 5300433	A	19940405	US 1991-765479	19910925	<--
PRAI	US 1989-366855		19890615	<--		
	WO 1990-US3355		19900613	<--		

AB Viruses are inactivated in blood products by treatment with a disinfectant, preferably NaSCN, in combination with a phys. process, preferably **ultrafiltration**. Human immunodeficiency virus-infected factor IX soln. (2 mL) was treated with 1 mL buffer (0.01 M Tris-HCl and 0.02 M EDTA, pH 8) and 1 mL 6 M NaSCN to inactivate the virus. Further inactivation occurred by **ultrafiltration**, using 6.2 nm **pore**-diam. membrane. The method does not cause protein denaturation.

IT **9001-27-8, Blood-coagulation factor VIII**
RL: BIOL (Biological study)
(virus inactivation in, by sodium thiocyanate and **ultrafiltration**)

L61 ANSWER 14 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1991:129076 HCAPLUS
DN 114:129076
TI Gel **filtration** for the purification of **blood coagulation factor VIII**
IN Hashimoto, Motonori; Noda, Munehiro; Motokubota, Toshiharu; Takechi, Kazuo; Yokoyama, Kazumasa
PA Green Cross Corp., Japan

SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 02255698	A2	19901016	JP 1989-79243	19890329 <--
	JP 2931319	B2	19990809		

AB A water-insol. **porous** gel is used to eliminate substances with mol. wt. 8 .times. 105-1 .times. 108 for the purifn. of **blood coagulation factor VIII**. The purified **coagulation factor** has a good soly. and can be prepd. as an effective medicine. Thus, crude **coagulation factor VIII** was prepd. from a cryoppt. of human **blood** and subjected to Sephacryl S-400 HR chromatog. to obtain the highly purified **coagulation factor**. The av. recovery of activity from the purifn. procedure was 75.4% and the sp. activity increased from 3.8 to 51.1.
IT **9001-27-8P, Blood-coagulation factor VIII**
RL: **PUR (Purification or recovery); PREP (Preparation)**
(purifn. of, from human **blood**, by gel **filtration**)

L61 ANSWER 15 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1991:30107 HCAPLUS
DN 114:30107
TI Removal of viruses from **blood-coagulation factor VIII** preparation
IN Osawa, Naoki; Hirasaki, Tomoko
PA Asahi Chemical Industry Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 02167232	A2	19900627	JP 1988-320349	19881221 <--
	JP 2832835	B2	19981209		
	JP 10337445	A2	19981222	JP 1998-131009	19881221 <--
PRAI	JP 1988-320349		19881221 <--		

AB Viruses are eliminated from **blood-coagulation factor VIII** (I) by **filtering** I through a **filter** made of regenerated cellulose **porous** membranes of hollow fibers. The method of **filtration** is described. Thus cellulose was dissolved 8% by wt. in a Cu-ammonia soln, **filtered**, defoamed, made into hollow regenerated cellulose fibers (inner diam. 250 .mu.m, membrane thickness 25 .mu.m, and **porosity** 39%). The hollow fibers (500 pieces) were bundled, and a I soln. at 2500 units/mL was **filtered** through the bundle at 1 mL/min to remove hepatitis B virus from the I soln.
IT **9001-27-8P, Blood-coagulation factor VIII**
RL: **PREP (Preparation)**
(virus removal from, by rayon **filter**)

L61 ANSWER 16 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1990:429231 HCAPLUS
DN 113:29231
TI Heat-stable **Factor VIII** concentrate
IN Oates, Adrian Malcolm
PA Commonwealth Serum Laboratories Commission, Australia
SO PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8909784	A1	19891019	WO 1989-AU154	19890407 <--
	W: DK, FI, NO, US				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	AU 8932583	A1	19891012	AU 1989-32583	19880408 <--
PRAI	AU 1988-7636		19880408 <--		

AB A heat-stable **factor** III conc. is prepd. from crude cryoppt. by subjecting the controlled **pore** glass (CPG) eluate to **diafiltration**. The CPG is prepd. by sepn. of **factor VIII** from plasma by cryopptn. and controlled **pore** glass chromatog. of the cryoppt. The CPG eluate was subjected to hollow-fiber **diafiltration**, using an equilibration buffer contg. 10 mM tris (pH 6.9), 10 mM tri-Na citrate, 100 mM NaCl, 1.5% sucrose and 1.2 mM **CaCl2**.

IT **9001-27-8P, Blood-coagulation factor VIII**
RL: **PREP (Preparation)**
(conc., heat-stable, prepn. of)

L61 ANSWER 17 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1989:550082 HCAPLUS
DN 111:150082
TI Adsorbents and method for purification of **blood-coagulation factor VIII**
IN Nagano, Yoko; Tani, Nobutaka
PA Kanegafuchi Chemical Industry Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 63209750	A2	19880831	JP 1987-42435	19870225 <--
	JP 04031735	B4	19920527		

AB Purifn. of **blood-coagulation factor VIII** uses a sulfate ester-contg., water-insol., **porous** gel adsorbent having a crit. exclusion mol. wt. of 8 .times. 106-1 .times. 109 and involves contacting the sample with the gel and elution. A **porous** cellulose gel (CK gel A-3) was dried and suspended in dehydrated pyridine, and to this was added chlorosulfonic acid. After stirring and **filtering**, the gel was washed to give a sulfated cellulose gel. Citric acid-contg. human **blood** plasma was passed through a column contg. the gel using saline as eluent to give a fraction contg. **factor VIII**.

IT **9001-27-8P, Blood coagulation factor VIII**
RL: **PUR (Purification or recovery); PREP (Preparation)**
(purifn. of, on sulfated adsorbent gel)

L61 ANSWER 18 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1988:576322 HCAPLUS
DN 109:176322
TI Blood products for parenteral administration, free of immunomodulator components
IN Eibl, Martha; Mannhalter, Josef; Leibl, Heinz
PA Immuno A.-G. fuer Chemisch-Medizinische Produkte, Austria
SO Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	EP 278948	A1	19880817	EP 1988-890028	19880208 <--
	EP 278948	B1	19920415		
	R: BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE				
	AT 8700299	A	19881215	AT 1987-299	19870212 <--
	AT 388501	B	19890725		
	CA 1306943	A1	19920901	CA 1988-557971	19880202 <--
	ES 2036720	T3	19930601	ES 1988-890028	19880208 <--
	NO 8800613	A	19880815	NO 1988-613	19880211 <--
	NO 175668	B	19940808		
	NO 175668	C	19941116		
	DK 8800738	A	19880813	DK 1988-738	19880212 <--
	DK 167844	B1	19931227		
	FI 8800684	A	19880813	FI 1988-684	19880212 <--
	FI 93516	C	19950425		
	JP 63203622	A2	19880823	JP 1988-31695	19880212 <--
PRAI	AT 1987-299		19870212 <--		

AB Title **blood** products, free of down-modulating activity on Fc receptors in leukocyte membranes, are prepd. by mol. sieving, such as by gel **filtration**, by treatment of the **blood** products with mol. sieves having immunomodulating components selectively adsorbed, or by **filtration** of the **blood** products through .ltoreq.10 nm **pore filters**. A **factor VIII** prepn. was incubated with staphylococcal protein A on Sepharose at pH 7.2 (citrate buffer) for 4 h, to give a product which, contrary to the starting prepn., did not significantly down-modulate the Fc receptor expression in monocyte membranes (Berken, A., et al., 1966).

IT **9001-27-8, Blood coagulation factor VIII**
RL: BIOL (Biological study)
(products from, for parenteral administration, free of down-modulating activity on Fc receptors in leukocyte membranes)

L61 ANSWER 19 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1985:154655 HCAPLUS
DN 102:154655
TI Methods for **factor VIII** preparation. II. Preparation of a high-purity concentrate by CPG
AU Perote, P.; Altamirano, P.; Aperador, R.; Camacho, Y.; Acosta, J.
CS Dep. Invest. Desarrollo, Lab. Landerlan, S. A., Madrid, Spain
SO Sangre (**1984**), 29(4-A), 457-66
CODEN: SNGRAW; ISSN: 0036-4355
DT Journal
LA Spanish
AB A method for **factor VIII** [**9001-27-8**] purifn. is presented. Cryoppts. are extd. with Tris [77-86-1] buffer, treated with Al(OH)3, pptd. at controlled pH and temp., and finally the external soln. is **filtered** through silica spheres of controlled **pore** of 550 .ANG. size (CPG). The product thus obtained is lyophilized and reconstituted at 25 U/mL. The biochem. characteristics of this product are studied by immunol. and electrophoretic techniques.

IT **9001-27-8P**
RL: **PUR (Purification or recovery); PREP (Preparation)**
(purifn. of)

L61 ANSWER 20 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1984:516625 HCAPLUS
DN 101:116625
TI A process for preparation of 'high-purity' **factor VIII** by controlled **pore** glass treatment
AU Margolis, J.; Gallovich, C. M.; Rhoades, P.
CS New South Wales Red Cross Blood Transfus. Serv., Sydney, Australia
SO Vox Sang. (**1984**), 46(6), 341-8
CODEN: VOSAAD; ISSN: 0042-9007
DT Journal
LA English

AB A simple process for large-scale manuf. of "high-purity" **factor VIII** [**9001-27-8**] is described in detail. A crude conc. prepd. from washed cryo is treated with controlled **pore** glass (CPG, 500.ANG. **pore** diam.) in proportion of 20-30 mL of CPG to 1 g input of protein. The slurry is poured into a sepn. column and the effluent purified conc. collected. The remaining **factor VIII** in the void vol. is displaced by a wash soln. After passage through a 0.2 .mu.m membrane **filter** the product is dispensed and lyophilized. Maintaining the operating pH at 6.5-6.7 and adding synthetic amino acids improved the yield and soly. The current conc. contains 1 unit of **factor VIII** per mg protein (10 units mg fibrinogen) with a recovery of 250 units/kg plasma. The CPG stage is nondestructive, yielding more than 90% of the input **factor VIII**.

IT **9001-27-8P**
RL: **PUR (Purification or recovery); PREP (Preparation)**
(purifn. of, controlled **pore** glass treatment in)

L61 ANSWER 21 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1984:73966 HCAPLUS
DN 100:73966
TI Concentrated preparation of antihemophilic factor of high purity
IN Jimenez Sanchez, Maxine Jesus
PA Laboratorios Hubber S. A., Spain
SO Span., 14 pp.
CODEN: SPXXAD
DT Patent
LA Spanish
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 511716	A1	19830701	ES 1982-511716	19820426 <--

AB **Factor VIII** [**9001-27-8**] of higher purity and virtually fibrinogen free was obtained by the purifn. of a cryoppt. of **blood** plasma at 0.5-1.0.degree. with Tris-HCl buffer 0.02M at pH 6.4-7.4 for 15-60 min, then the **Factor VIII** is extd. from the cryoppt. with tris-HCl buffer at 14-25.degree. for 20-60 min. The prothrombin complex is deactivated with Na **heparin** (0.1-5 U.S.P units/mL soln.). Fibrinogen is pptd. first with Na citrate 0.02M at pH 6.0-6.5 and then with polyethylene glycol 4000 (4-5%) at 14-25.degree. for 15-40 min. The ppt. is centrifuged and the supernatant is **filtered** through **filters** of **pore** size 8.0, 3.0, and 1.2 .mu.. To this **filtrate**, polyethylene glycol 4000 is added up to a concn. of 10-12% to ppt. **Factor VIII** at 15-25.degree. for 15-40 min. The paste contg. **Factor VIII** is washed with Tris-HCl 0.02M, pH 6.8 and 8% EtOH at -5 to 0.degree.. The **Factor VIII** paste is dissolved in citrate buffer p(pH 6.8-7.2) 0.03M in a ratio of 45-55 mL buffer/g paste. An antihemophilic **factor** of high purity is thus obtained. An example is given in which the above procedure is followed to obtain a highly purified **Factor VIII** which is highly conc. and has a specific activity of .apprx.3 units **Factor VIII** /mg protein.

IT **9001-27-8P**
RL: **PREP (Preparation)**
(conc., purifn. of)

L61 ANSWER 22 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1982:488182 HCAPLUS
DN 97:88182
TI **Microporous** membranes and crossflow **filtration** of macromolecules and particles
AU Lindley, P. D.; Olson, W. P.; Faith, M. R.
CS Hyland Ther. Div., Travenol Lab., Los Angeles, CA, 90039, USA
SO Polym. Sci. Technol. (**1982**), 16(Polym. Sep. Media), 173-90
CODEN: POSTB5; ISSN: 0093-6286

DT Journal
LA English
AB Crossflow **filtration** (a procedure in which a proportion of the feed sweeps contaminating particles from the **filter** surface) with 0.2 .mu.m-rated polymeric membrane **filters** alleviated the problems of viscosity-imposed limits to flux, flow decay caused by protein adsorption, and **pore** occlusion by particles. Crossflow **filtration** of albumins, antihemophilic factor, and yeast was studied.
IT **9001-27-8**
RL: ANST (Analytical study)
(**filtration** of, crossflow, on polymeric membrane **filters**)

L61 ANSWER 23 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1981:71468 HCAPLUS
DN 94:71468
TI Side reaction-free plasma fractions
IN Eibl, Johann; Elsinger, Fritz; Linnau, Yendra
PA Immuno A.-G. fuer Chemisch-Medizinische Produkte, Austria
SO Austrian, 8 pp.
CODEN: AUXXAK
DT Patent
LA German
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	AT 359646	B	19801125	AT 1979-2940	19790419 <--
	AT 7902940	A	19800415		
	JP 55141414	A2	19801105	JP 1980-49124	19800414 <--
	JP 60028812	B4	19850706		
	EP 18353	A1	19801029	EP 1980-890044	19800415 <--
	EP 18353	B1	19840125		
	R: BE, CH, DE, FR, GB, IT, LU, NL, SE				
	US 4388232	A	19830614	US 1982-375044	19820505 <--
PRAI	AT 1979-2940		19790419 <--		
	US 1980-135234		19800331 <--		

AB Plasma fractions, esp. **coagulation factors**, free of side reactions were prepd. by fractionation and purifn. in the presence of **Ca**-binding anticoagulants and fast-reacting antithrombin [9000-94-6] (0.5-50 units/mL). The fast-reacting antithrombin was formed in situ by addn. of **heparin** or heparinoids. Thus, 10.8 L frozen citrated human plasma was thawed at 0-2.degree. and the cryoppt. (100 g) was collected by centrifuging, dissolved in 400 mL pH 7.5 0.2% citrate buffer at 37.degree. and mixed with preformed fast-reacting antithrombin to give a concn. of 6 units/mL. The antithrombin was formed from 73.5 mL plasma and 147 IU **heparin**. The cryoppt. soln. was mixed with 19.6 mL 3% Al(OH)3 suspension, stirred 30 min at room temp., and centrifuged. The supernatant was mixed with addnl. preformed antithrombin to replace that adsorbed by Al(OH)3, and EtOH was added to 7% concn. to ppt. inactive proteins. The ppt. was centrifuged, EtOH was added to the supernatant to 10% concn., the temp. was reduced to -2.degree. to ppt. **blood coagulation factor VIII** [**9001-27-8**]. The ppt. was dissolved in 0.5% saline contg. 0.2% citrate, 1.0% glycine, and the antithrombin was added to 6 units/mL. The soln. was **filtered** through a membrane with 0.2 .mu.m **pores** and lyophilized.
IT **9001-27-8P**
RL: **PREP (Preparation)**
(prepn. of, free of side reactions)

L61 ANSWER 24 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1979:598833 HCAPLUS
DN 91:198833
TI Preparation of stable intermediate-purity **factor VIII** concentrate with a note on high-purity **factor VIII**

AU Margolis, J.; Rhoades, P.
CS Red Cross Blood Transfus. Serv., Sydney, Australia
SO Vox Sang. (**1979**), 36(6), 369-74
CODEN: VOSAAD; ISSN: 0042-9007
DT Journal
LA English
AB Cryoppt. prepd. by a rapid thawing technique was pooled in batches of 600-720 donor units and washed with ice-cold Tris-citrate-NaCl soln. After dissolving at 37.degree., it was adsorbed with Al(OH)3 and kaolin, and cleared by centrifugation. The supernatant, dild. with 5% dextrose was passed repeatedly through a bed of Celite, **filtered** through a 293 mm .times. 0.3 .mu.m membrane disk and lyophilized. A typical compn. was 15 U.cntdot.mL-1 **factor VIII** [**9001-27-8**], and 40 mg.cntdot.mL-1 protein with a yield of 300 U/L of starting plasma. The crude **factor VIII** conc. was also suitable material for prepn. of high-purity **factor VIII** by controlled **pore** glass chromatog.
IT **9001-27-8P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of stable intermediate-purity)

L61 ANSWER 25 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1979:451363 HCAPLUS
DN 91:51363
TI Studies on **factor VIII**-related protein. I. Ultrastructural and electrophoretic heterogeneity of human **factor VIII**-related protein
AU Beck, Eugene A.; Tranqui-Pouit, Leone; Chapel, Agnes; Perret, Beat A.; Furlan, Miha; Hudry-Clergeon, Gilbert; Suscillon, Michel
CS Cent. Hematol. Lab., Inselspital, Bern, Switz.
SO Biochim. Biophys. Acta (**1979**), 578(1), 155-63
CODEN: BBACAQ; ISSN: 0006-3002
DT Journal
LA English
AB Human **factor VIII** was purified from its cryoppt. by subsequent gel **filtration** on crosslinked large-**pore** agarose. **Factor VIII**-related protein appeared as a large aggregate following electrophoresis on 3% polyacrylamide gels in the presence of Na dodecyl sulfate (SDS). The same material was sepd. into multiple bands (mol. wt. in excess of several millions) following electrophoresis on SDS-1% agarose gels. After complete SS redn. of **factor VIII**-related protein and electrophoresis on SDS-5% polyacrylamide gels, a single subunit chain (mol. wt. 200,000) was revealed. Anal. of this protein in its nonreduced state by neg. contrast electron microscopy showed filaments of markedly variable size. The calcd. mol. wt. of such filaments ranged from .apprx.0.6 .times. 106 to 20 .times. 106. Size heterogeneity is apparently an essential feature of human **factor VIII**-related protein.
IT **9001-27-8**
RL: BIOL (Biological study)
(aggregates of and size heterogeneity of)

L61 ANSWER 26 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1978:79095 HCAPLUS
DN 88:79095
TI Method and apparatus for manufacturing sterile **filtered** blood coagulation factors
IN Seufert, Arnold
PA Ger.
SO Ger. Offen., 22 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 5

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI	DE 2624373	A1	19771208	DE 1976-2624373	19760531 <--
	DE 2624373	C2	19830203		
	AT 7703244	A	19800715	AT 1977-3244	19770506 <--
	AT 361123	B	19810225		
	CH 626252	A	19811113	CH 1977-5794	19770509 <--
	NL 7705655	A	19771202	NL 1977-5655	19770523 <--
	FR 2353298	A1	19771230	FR 1977-16150	19770526 <--
	FR 2353298	B1	19820618		
	DD 131452	C	19780628	DD 1977-199165	19770526 <--
	US 4141887	A	19790227	US 1977-800776	19770526 <--
	GB 1571202	A	19800709	GB 1977-22192	19770526 <--
	SE 7706272	A	19771201	SE 1977-6272	19770527 <--
	SE 444646	B	19860428		
	SE 444646	C	19860807		
	JP 52148610	A2	19771210	JP 1977-61322	19770527 <--
	ZA 7703208	A	19780530	ZA 1977-3208	19770527 <--
	ES 459263	A1	19780316	ES 1977-459263	19770528 <--
	CA 1088424	A1	19801028	CA 1977-279448	19770530 <--
	BE 855187	A1	19770916	BE 1977-55954	19770531 <--
	AU 7725662	A1	19781207	AU 1977-25662	19770531 <--
	AU 514223	B2	19810129		
	CS 244662	B2	19860814	CS 1981-5879	19810803 <--
PRAI	DE 1976-2624373		19760531 <--		
	CS 1977-6414		19771004 <--		

AB An efficient, economical procedure for prepg. sterile-**filtered** **blood-coagulation factors** with a high concn. of **factors** I or **VIII** [**9001-27-8**] and carrying a min. risk of hepatitis consists of sepg. the plasma of 1 or a few donors almost abs. from cellular components, freezing the purified plasma at <-22.degree., thawing at .apprx.2.degree., sepg. the cryoppt. (having an enriched **factor VIII** content) by centrifugation, dissolving the cryoppt. in buffer, and sterile-**filtering** in an autoclaved **filter** app. The supernatant from the cryoppt. can be used as a source of fibrinogen. A sterile-**filtration** app. is described which consists of a pressure housing contg. a series of membrane **filters** of decreasing **pore** size, the smallest of which is 0.22 .mu.m. To retard clogging the **filters**, the application of pressure is at 90.degree. to the liq. flow.

IT **9001-27-8P**
RL: **PREP (Preparation)**
(isolation and purifn. of, from blood plasma, sterile-**filtration** app. for)

L61 ANSWER 27 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1976:556140 HCAPLUS
DN 85:156140
TI Device and method for withdrawing **blood** and separating a cryoprecipitate rich in **Factor VIII**
IN Garber, J. W.; Davisson, D. W. G.
PA Baxter Laboratories, Inc., USA
SO Belg., 17 pp.
CODEN: BEXXAL
DT Patent
LA French
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	BE 832979	A1	19751231	BE 1975-159663	19750902 <--
	US 3986506	A	19761019	US 1974-503018	19740903 <--
	ZA 7505396	A	19760728	ZA 1975-5396	19750822 <--
	AU 7584320	A1	19770303	AU 1975-84320	19750827 <--
	FI 7502421	A	19760304	FI 1975-2421	19750828 <--
	DK 7503907	A	19760304	DK 1975-3907	19750829 <--
	JP 51051513	A2	19760507	JP 1975-105581	19750829 <--
	SE 7509749	A	19760304	SE 1975-9749	19750902 <--

	NO 7503004	A	19760304	NO 1975-3004	19750902 <--
	FR 2283700	A1	19760402	FR 1975-26927	19750902 <--
	DE 2539010	A1	19760408	DE 1975-2539010	19750902 <--
	BR 7505623	A	19760803	BR 1975-5623	19750902 <--
	ES 440695	A1	19770816	ES 1975-440695	19750903 <--
PRAI	US 1974-503018		19740903 <--		
	US 1975-545067		19750129 <--		

AB A device and process for obtaining **blood-coagulation factor VIII** from **blood** plasma are described that involve cryopptn. The device for sampling and treatment of the **blood** consists of a closed container with a **filtration** bed of **porous** polyurethane foam at the aperture that retains the **factor VIII**-rich cryoppt. The device also contains a series of closed containers interconnected by flexible conduits, the 1st container equipped with **blood** sampler, being attached to the interior container with **filtration** bed where the **blood** is frozen, thawed, (preferably at <20.degree.), and collected. This compartment is attached to a 3rd container for the aseptic collection of plasma depleted of cryoppt. The **filter** bed is washed with physiol. saline to then obtain the **factor VIII**-rich cryoppt.

IT **9001-27-8**
RL: ANST (Analytical study)
(sepn. of, from blood plasma, app. and methods for)

L61 ANSWER 28 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1975:560327 HCAPLUS
DN 83:160327
TI **Extracorporeal blood filters.** Alterations of total lactate dehydrogenase and isoenzyme activity and of **coagulation factors** I and **VIII** under arterial flow condition
AU Herzer, J. A.; Krian, A.; Schulte, H. D.; Bruester, H.; Bircks, W.
CS Chir. Klin. Poliklin., Univ. Duesseldorf, Duesseldorf, Ger.
SO Chir. Forum Exp. Klin. Forsch. (**1974**) 179-83
CODEN: CFEKA7
DT Journal
LA German
AB Two different types of **extracorporeal blood filters** were examd. in a recirculation system in order to investigate possible secondary effects. Therefore, the activity of 2 lactate dehydrogenase isoenzymes and the level of fibrinogen and **factor VIII** were detd. several times during the investigation. An alteration of the protein mols. was found and proteins were found free in the **blood** stream. It was concluded that proteins were adhesively **filtered**. These secondary effects were a function of the dimensions of the total **filter** surface.
IT **9001-27-8**
RL: ANT (Analyte); ANST (Analytical study)
(detn. of, **extracorporeal** blood **filtration** in relation to)

L61 ANSWER 29 OF 29 HCAPLUS COPYRIGHT 2001 ACS
AN 1967:9221 HCAPLUS
DN 66:9221
TI Hemostatic fraction of the plasma containing four factors (II, VII, IX, X) of the blood coagulation system
AU Steinbuch, Marion; Soulier, Jean P.
CS Natl. Center Blood Transfusion, Paris, Fr.
SO Probl. Gematol. Pereliv. Krovi (**1966**), 11(10), 15-21
CODEN: PGPKA8
DT Journal
LA Russian
AB To prepare the so-called PPSB fraction of **blood** plasma, which contains the title **factors**, citrate must not be used to stabilize the **blood**, since citrate inhibits the adsorption of

anticoagulation **factors** on Ca3(PO4)2. Mix 350-400 ml. **blood** no older than 48 hrs. with 50 ml. EDTA soln. (Na2H2EDTA 6 g., NaCl 6.9 g., water 1000 ml.), centrifuge, add 0.5% Ca3(PO4)2 to the plasma, let stand for 15 min. at room temp., and elute twice with 0.18M citrate soln. (1/20 and 1/40 of the initial plasma vol., resp.) at room temp. within 30 min. Add tetracycline (50 mg./l.) to prevent contamination and let stand overnight at 0.degree.. Dil. with an equal vol. of distd. water (pH 6.8, 0.degree.), add 95% EtOH (precooled) until its concn. is 16% (final temp. must be -4.degree.), and sep. the ppt. which contains labile lipoproteins. Decrease the pH of the supernatant to 5.2 and increase EtOH (precooled) concn. to 25% (-7.degree.); the formed ppt. contains the active title **factors**. Dissolve in a mixt. of 9 vols. 0.5% NaCl and one vol. 0.1M citrate, using 1/80 of original plasma vol., hold the pH at 6.8, and add 10 mg. **heparin**/100 ml. vol. **Filter** and sterilize by **filtration** (**pore** diam. 0.45 .mu.). Lyophilize 10 or 25 ml. portions and do not exceed 25.degree.. The PPSB fraction does not contain **factor VIII** nor V, and **factors** II, VII, IX, and X were concd. 10-40-fold. 15 references.